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“Making Translation Happen”

Translating Neurobiological Research

Research Report

December 2009

Report prepared by Jim Ottaway for the

BIOS Centre for the Study of Bioscience, Biomedicine, Biotechnology and Society

London School of Economics and Political Science

Table of Contents

Preface.....	4
Executive Summary.....	5
1. Introduction.....	11
<i>The Cooksey Report</i>	<i>11</i>
<i>The UK Medical Research Council</i>	<i>14</i>
<i>Evaluating the success of translation</i>	<i>16</i>
<i>The current study.....</i>	<i>20</i>
Background to our approach.....	21
The timescale of scientific research	21
The diversity of criteria to judge value: value for whom?.....	22
The context and role of evaluation in a ‘knowledge based economy’	23
The Role of the Translational Imperative in a Post-Audit Society.....	24
<i>Choice of case study.....</i>	<i>25</i>
<i>Data gathered.....</i>	<i>27</i>
Literature on translational research	27
Interviews with stakeholders in biomedical translation.....	28
Interviews with researchers at the IoP.....	28
Bibliometric analysis	29
2. Translational research: history, models, and methods of evaluation.....	30
3. Stakeholder views of translational research.....	38
<i>Examples of successful translation</i>	<i>38</i>
<i>The culture of basic science</i>	<i>42</i>
<i>Research vs. advocacy.....</i>	<i>43</i>
<i>Beyond the metaphor of barriers</i>	<i>46</i>
<i>Conclusion.....</i>	<i>47</i>
4. Translation at the IOP	49
<i>What is translation?</i>	<i>51</i>
<i>Translation may threaten the importance of basic research at this stage in psychiatry.....</i>	<i>57</i>

<i>The role of the SGDP – gene-environment interaction</i>	59
<i>It is just presentational</i>	60
<i>It's important, but not my job</i>	61
<i>You can't build it in – indeterminacy</i>	63
<i>It's changed the way I think</i>	66
<i>Translation in practice</i>	67
<i>Translation in a system of worth</i>	70
<i>Translation and interdisciplinarity</i>	72
<i>Conclusion</i>	75
5. Bibliometric Findings on Translation at the SGDP	78
<i>Bibliometric data</i>	78
<i>Classification of publications from clinical to basic: the research level indicator</i>	79
<i>Orientation of journals for the publication of SGDP research</i>	81
<i>Sources of SGDP research – citation analysis</i>	89
<i>Impacts of SGDP research – citation analysis</i>	91
<i>External collaboration from researchers at the SGDP</i>	94
<i>The balance of basic and clinical publication for individual authors</i>	96
<i>Interdisciplinarity and collaboration</i>	99
<i>Discussion</i>	105
6. Conclusions	108
Bibliography	112
APPENDIX ONE: Interview topic guide	115
Endnotes	116

PREFACE

The BIOS Centre for the Study of Bioscience, Biomedicine, Biotechnology and Society was approached by the MRC and Kings College London in the Summer of 2006 to undertake a qualitative case study of the outcome of MRC funded research at King's, drawing on insights from the social studies of science and technology, and from historical and ethnographic studies of research in the life sciences. Following discussion it was agreed this would take the form of a case study of the Social, Genetic and Developmental Psychiatry Centre, at the Institute of Psychiatry, which is part of King's College. The study was undertaken by Dr Jim Ottaway under the overall direction of Professor Nikolas Rose, Professor Sarah Franklin and Dr. Ilina Singh. The study was advised by a Steering Group whose members were Professor David Armstrong, Professor Martin Knapp, Dr. Grant Lewison, Professor Jack Price, Professor George Szumukler, and Professor Andrew Webster. We would like to thank members of the Steering Group for their helpful comments on an earlier draft of this paper; however full responsibility for the argument and the conclusions remains with the authors.

EXECUTIVE SUMMARY

1. The BIOS Centre for the Study of Bioscience, Biomedicine, Biotechnology and Society at the London School of Economics and Political Science was approached by the MRC and Kings College London in the Summer of 2006 to undertake a qualitative case study of the outcome of MRC funded research at King's, drawing on insights from the social studies of science and technology, and from historical and ethnographic studies of research in the life sciences. Following discussion it was agreed this would take the form of a case study of the Social, Genetic and Developmental Psychiatry Centre (SGDP), at the Institute of Psychiatry, which is part of King's College. The research involved analysis of relevant policy and academic literature, interviews with stakeholders, interviews with researchers at the SGDP and a bibliometric study of publications from researchers based at the SGDP.

2. Translation in this context principally refers to the process by which advances in basic research in the life sciences give rise to benefits to patients in treatment or prevention of disease and/or gives rise to commercial products which generate economic benefits to the parties involved, as well as to direct patient benefit through their take up and use. In the field of medicine, the current debate over translation is grounded on a widespread perception that significant public investment in research in the life sciences from the 1960s to the present has not generated the anticipated, and promised, advances in clinical medicine or health care.

3. Early views of translation tended to picture a linear process whereby basic research gave rise to applied research which then led to development of therapies or products which then diffused into the clinic or the production process. This picture has proved to be misleading, and the problems with this conception have generated much academic and policy debate, and led to the emergence of a more complex picture of the interactive relations involved. These have been embodied in important changes in the

strategies adopted by biomedical funding agencies such as the Medical Research Council in the UK and the National Institute of Health in the US. These indicate that a more complex and nuanced understanding of the process of translation is taking shape, more aware of the institutional forces that need to be mustered and shaped in order to nudge basic researchers, research funders and clinical practitioners into closer and more productive relations.

4. There are differences in opinion among stakeholders as to the nature and relevance of the current 'translational imperative' in biomedicine in general and psychiatry in particular. Some point to specific examples of successful translation and suggest that these can function as generalizable models. For example the very influential Cooksey Report in the UK published in 2006 pointed to the development of 'DNA fingerprinting' and the isolation and reproduction of monoclonal antibodies, each of which seem to exemplify a fairly direct, specific and rapid pathway from a single discovery or set of discoveries in the laboratory to application in clinical or other settings and indeed to industrial development. However those closest to the specific domain of our case study expressed a level of scepticism about the generalizability of such a model, pointing to the long timescales that typified most cases in which laboratory findings had led to clinical developments, the fact that in many cases findings outside the laboratory, for example in epidemiology, were crucial, that in most cases it will be difficult if not impossible to judge what clinical applications might follow from basic research, and hence that translational benefits may be placed most at risk by an "ill-considered rush" from laboratory findings to randomised controlled trials to adjudicate efficacy. Further, there was a view that the most significant translational outcomes of this type of research might be found in changes in social policy and policies for public health, rather than in direct clinical applications. Thus key senior actors at the SGDP argued that what was required was carefully considered hypothesis-based bridging research, located in the context of two-way transactions, to

determine whether, and how, research findings may have clinical or public health implications.

5. Such insights into the views of key participants leads us to suggest that in order to understand the success of models of translation as they affect, or capture, the conduct of research itself, it may be necessary to undertake a deeper exploration of the cultures, beliefs and expectations of the actors involved in 'making translation happen'. In the light of this we propose a model in this Report which locates translational research within the 'economies of worth' of different participants, and explores their modes of justification of the worthiness of research. That is to say we have empirically documented the ways in which researchers situate themselves in relation to the demands of translation, and understand the pathways from research to outcomes. In turn, this approach helps to illuminate how researchers adopt, or reject, a disposition to produce 'translation situations' in the way in which they go about their research activities in practice, and what factors influence them to do so.

6. Our qualitative research revealed a wide variety of beliefs about, and attitudes towards, the translational imperative among the researchers themselves. We group these into five general themes:

- *Rhetoric*: Translation here is seen either as a piece of jargon currently in fashion, or as a way of re-describing research as a means of securing funding.
- *What we have always done*: Translation here is seen is a term applied to what basic scientists have always done, which is to aim to produce results that have practical implications.
- *Fundamental*: All research should be translational in its aims; research should not be done for research's sake or for its curiosity-value.
- *Orthogonal*: Translational goals are different from those of basic research; they may, however, be linked together in such a way that advancement of scientific knowledge also produces benefits, albeit as a side-effect.

- *Translation versus application:* Translation, in its widely accepted form, confuses two distinct processes: applications (treatments, for example) and the propagation of findings from one field to another.

7. These findings confirm that even in one rather narrow branch of potentially translational biomedical research, the psychiatric research carried out in one centre of one specialised psychiatric research institute, there is little agreement about what constitutes translation, let alone on how it should best be achieved. Individual views can best be understood by locating the translational disposition of actors within their own individual systems of worth, the way in which they chose, justify and legitimate their own activities and research priorities, and the way in which they give meaning to these activities in their narratives, which are fundamental to their identities as researchers. If the imperative of translation is itself to translate into the activities of those actually undertaking the research, the success of this process will depend on the ability of all those involved to both recognise, and to align, the diverse economies of work that characterise the research environment. Overall, our qualitative research indicates that while almost all researchers at the SGDP are crucially concerned with, and committed to, the significance of their research for the improvement of individual and collective mental health, many do not feel that they themselves are the most appropriate people to take their research down the translational pathway, or to be responsible for the ways in which it is taken up and used. Further, even among those most committed to the value of translation, there is considerable scepticism about the ways in which the translational imperative might be embedded within a growing culture of audit and evaluation and the potential consequences.

8. Our bibliometric analyses show that the publications of SGDP researchers do indicate a significant interest in translational potential, and one that increases over the period since the Centre was established, the majority of publications being directed to the borders between the clinical and clinical mix categories, indicating a concern with

the potential applicability of the findings and to communicating research results into the clinical domain. This is consistent with the espousal of many researchers at the SGDP with the model of 'experimental medicine' developed by senior figures at the SGDP. Over the period from 1990 to the present the collaborative emphasis of the SGDP, embodied in the very design of the institution and its physical form, has facilitated an increasing level of interdisciplinary collaboration between research on the social, developmental and genetic aspects of behaviour among researchers based and this embodies on key dimension of translation. It also suggests that it is insufficient to judge translational outcomes by focussing solely on publication outputs over the short or even medium term. There is a need to develop more sophisticated and sensitive methods for capturing the impacts of research funding in relation to the generation of economic and health benefits, and the multiple forms that such impacts can take. The pathways from research outputs to policy are particularly difficult to capture, given the different timescales on which they operate, the heterogeneous factors that affect the take-up of research findings in debates over policy, and the socio-political and economic vicissitudes that shape the process of policy formation and change.

9. In sum, it is clear from our research that there are multiple models of translation at work among researchers, and multiple overlaps and divergences between researchers and those in managerial and policy roles. This plurality arises from the research and institutional context itself, and the variety of values, roles, orientations and objectives of the different participants. While such plurality is to be expected, our findings show it can be characterised and schematised in a manner that illuminates key factors influencing established 'cultures of translation'. Hence we would argue that the aim of government and research funders should not be to seek to reconcile all of these diverse translational rationales, but to 'adjust' them to the different contexts for which they are relevant. Governments and funding agencies do not need to utilise the same definitions of 'successful translation' as those adopted by the researchers in any one area, but they do need a vocabulary and some techniques to enable them to intervene

in these situations and shape them in particular directions, while recognising their specificity and without distorting them to fit external or artificial demands of audit. In this sense 'translation' comes to resemble 'transparency' – framed in a very wide and inclusive sense it can become a language to which all can subscribe, and within which all can adjust their ways of working so that they are loosely coupled together towards the same overall ends.

10. Further, we suggest, while few would argue with the underlying hopes and aspirations that have led to the current emphasis on translation, there may be some dangers in raising expectations of rapid translation, increasing pressures on researchers to exaggerate or oversimplify the pathway from basic research to clinical application, and perhaps leading to disillusionment among the public and among policy makers about the long term value of investment in basic biomedical research.

1. INTRODUCTION

The question of 'translation' has attained increasing prominence in relation to biomedical research over the last decade. In this context, translation principally refers to the process by which advances in basic research in the life sciences give rise to benefits to patients in treatment or prevention of disease. In addition to the pathway to direct patient benefit, translation refers to the process by which research gives rise to commercial products, such as pharmaceuticals, which generate economic benefits to the parties involved, as well as to direct patient benefit through their take up and use. In the field of medicine, the current debate over translation is grounded on a widespread perception that significant public investment in research in the life sciences from the 1960s to the present has not generated the anticipated, and promised, advances in clinical medicine or health care. In the first decade of the twenty first century, this perception led to a number of developments in the UK to examine this issue and to seek to overcome barriers to translation.

The Cooksey Report

In the UK, the perceived translation deficit led to an invitation, in March 2006, from the Chancellor of the Exchequer and the Secretaries of State for Health and Trade and Industry to Sir David Cooksey to undertake an independent review to advise on the best design and institutional arrangements for the public funding of health research in the UK. Cooksey's review of UK health research funding (hereafter the Cooksey Report) was published in December 2006. The report acknowledged the numerous initiatives in the UK commissioned to ensure a strong infrastructure for maximising translational benefits to both the public and private sectors (Cooksey 2006: 3), noting that:

the UK Government has taken a number of actions to ensure the UK remains at the forefront of health research and a location of choice for the pharmaceuticals industry to locate its R&D. These actions include the creation of the UK Clinical Research Collaboration (UKCRC) to improve the infrastructure for clinical and medical research; the creation of the Joint MRC/NHS Health Research Delivery Group in the 2004 Spending Review to enable a more joined up approach between Government funders of medical and clinical research; the creation of a new strategy for research in the NHS in England, *Best Research for Best Health* (BRfBH); and the establishment of MRC Technology, to manage and commercially develop intellectual property arising from the basic research carried out by the MRC's directly-supported scientists.

However it concluded that the UK was at risk of failing to reap the full economic, health and social benefits that its public investment in health research should generate, and that there was no overarching UK health research strategy to ensure UK health priorities are considered in all relevant research. Further it argued that there were "two key gaps in the translation of health research: translating ideas from basic and clinical research into the development of new products and approaches to treatment of disease and illness; and - implementing those new products and approaches into clinical practice." (Cooksey 2006: 3) It is these translational gaps which remain the subject of vigorous debate in the UK.

Cooksey identified numerous cultural, institutional and financial barriers to translation in research that was publicly funded, as well as challenges faced by the pharmaceutical industry in efforts by the private sector translating research into health and economic benefit. Among the cultural barriers it noted the belief that research proposals for funding should be evaluated by scientists themselves, not by the governmental bodies that are themselves responsible for the funding. It also recognised professional disincentives for scientists such as the higher status accorded to publications in prestigious journals that favour basic research, often making rather superficial reference to the potential health benefits and clinical applications, while translational research tends to be published in more specialised journals of lower status. It argued that applied and translational research thus often faced greater obstacles attaining

favourable judgments in the peer review process. It noted the difficulties faced by clinical health researchers in managing the twin, and potentially conflicting, requirements of their scientific research and their clinical practice. It identified various institutional and financial barriers to translational research, including the separation of research supported by the health department from that supported by the MRC, and a more general lack of coordination between the different institutional and commercial stakeholders. For these and other reasons it also emphasised the difficulties that have been faced in attempts to evaluate the relative contributions of laboratory-instigated research and clinic-instigated research (Cooksey 2006: 40). Thus, it concluded,

advances from biomedical research may have different development timeframes from those of clinical research. The investment requirements also tend to be different in each case. Moreover, the types of therapeutic advance may differ depending on the origins of the research. For example, laboratory-instigated research may be more likely to lead to improved drug treatments, while clinic-instigated research may produce more interventions based on devices....”

Given the range of difficulties hampering more robust evaluation of translational outcomes convincingly identified by the Report, it was in some respects surprising its conclusions amplified the call by many of those who it consulted for new systems or methodologies to underpin the systematic review of existing research, for improved and more consistent methods of evaluation. However, a primary recommendation of the Cooksey report was that “such ‘research on research’ should help to inform policy decisions on how limited resources can deliver new knowledge where it is most likely to have substantial impact in addressing unmet medical needs” (Cooksey 2006: 40-1)

Following the Cooksey Report, the Comprehensive Spending Review of 9 October 2007 announced a 28.5 percent increase in funding for medical research from £543.4 million in 2007–08 to £ 707 million in 2010–11, plus nearly £1 billion for the National Institute for Health Research. As reported in the *Times* on 10 October 2007, the bulk of this new money was to be “targeted at “translational” research projects, which aim to turn basic medical discoveries into drugs and treatments. ... The extra support means that basic

research funding should not have to be cut to accommodate the fresh emphasis on translation recommended by Sir David Cooksey last year in a root-and-branch review of support for medical science.”. And, according to the Times report “Independent medical research groups also welcomed the settlement. Professor Sir Michael Rutter, vice-president of the Academy of Medical Sciences, said: “This substantial increase in funding will position the UK as a world leader in basic medical science and clinical research. It will support fundamental research into the major underlying questions of health and disease and, importantly, the translation of that research into benefits for patients.”¹ Cooksey convincingly identified many barriers to translation and concluded that, as the process remained poorly understood, better measures for evaluating its efficacy should be developed.

The UK Medical Research Council

In the UK, the issue of translation has been of particular significance for the Medical Research Council, whose mission, as set out in its mission statement (Medical Research Council 2009) is to:

- Encourage and support high-quality research with the aim of improving human health.
- Produce skilled researchers, and to advance and disseminate knowledge and technology to improve the quality of life and economic competitiveness in the UK.
- Promote dialogue with the public about medical research.

In 2004, the MRC entitled its Annual Review *Translating Research* (MRC 2004), and in the Introduction, Colin Blakemore, then Chief Executive, trod a careful path, insisting that the MRC “has always been guided by its principle of supporting the very best science” and giving examples of funded research that “may not seem immediately relevant to health” and acknowledging that “[m]any of our units and institutes are ... in the early stages of the translation pipeline” while stating that (MRC 2004: 1):

Over the coming years we intend to accelerate the rate at which MRC research is translated into new methods of diagnosis and treatment – a process that can take anything from a few years to decades.

Another key element, relevant to Cooksey's later emphasis, was the attention given to the need to "work... closely with the pharmaceutical and biotech companies to bring our knowledge and discoveries into the healthcare system and so to patients" notably by licensing discoveries that can then be taken up by commercial companies to make new products (MRC 2004: 1). While this report does not give detailed attention to the process of translation itself, the general view adopted seems to be that of a linear model from discovery to treatment, for example suggesting that, in the case of neurodegenerative diseases such as Alzheimer's and Parkinson's, "We shall be looking to advances in molecular and cell biology to help us understand the causes at a fundamental cellular level, which will in turn guide the development of new forms of treatment, including cell therapies" (MRC 2004: 2).

In the subsequent years, leading up to and beyond the Cooksey Report, the MRC devoted considerable attention to the ways in which it could best enable translation, including commissioning Ernst and Young to carry out a strategic review of its organization (Ernst and Young 2007). This review concluded that while the MRC had great strengths, notably high standards of scientific appraisal of research programmes and initiatives; support for long-term and multidisciplinary science, and for outstanding individuals; excellent quality in research and innovation in its institutes and units; and the MRC Technology (MRCT) and related initiatives in applied research and development and venture capital funding, "the health research system in which MRC operates is undergoing a major change with an increasing expectation that policies and funding will ensure knowledge from discovery science 'translates' into health and wealth benefits" (Ernst and Young 2007: 1) The review concluded that the "MRC needs a 'step change' in its organisational capability and culture" that should

“better set and communicate strategy, clearly articulating what it funds, why, and how this will result in health and wealth benefits for the UK ... [and] put in place measures of outcomes and benefits at policy, programme, and award level to better evaluate return on investment (ROI”. It should also “invest in building a core competency and culture in managing research and training for translation” (Ernst and Young 2007: 2). Among other organizational changes, the review recommended that “MRC should invest more in clarifying, communicating, measuring and incentivising the activities that add most to health and wealth benefits... [and] should look for greater clarity on benefits for all its research, while creating specific funding routes, with different evaluation and management approaches, for its more goal-oriented research.” (Ernst and Young 2007: 2). The report concluded that MRC should become a body that “can set the international benchmark as a health research body that not only delivers world class research with a purpose – funding and influencing discovery research and training but that “champions translation”, is “effective in building closer links between discovery science and more developmental or translational research and in fostering links to users” and demonstrates “clear return on investment” by communicating what it funds, why, and what the resulting, health and wealth benefits are to the UK. This emphasis on more effective measurement of translational outputs echoes the conclusion reached by Cooksey. It also implies that what is required to enhance translational efficacy is more robust management and greater accountability. However, if it is the case that the actual process of translation is not well understood, exhortations to manage translation better without a clearer sense of how translation actually happens may be premature.

Evaluating the success of translation

The Cooksey Report, the government, and the Ernst and Young advisors thus all identify improved translation as a critical goal, offering somewhat different approaches. For Cooksey, the approach is scientific: more basic knowledge of the

translation process needs to be gathered in order to improve translational outcomes. The Government, responding to this advice, dedicated resources with a broadly translational intent, but funded no specific programmes of research into translation itself. A stronger managerial culture was advocated by the private sector consultants Ernst and Young, but, again, no clearer evidence based understandings of the translational process were offered, and thus the underlying process to be improved, and the problems to be solved, remained unclear. The most obvious approach to this dilemma is indeed the most common: to seek to measure the extent to which translation has occurred and medical research has resulted in different kinds of benefits. Many organizations have recently addressed the challenges of evaluating the benefits of medical research, and a sub-discipline has developed around these issues. A UK evaluation forum has recently reviewed these methods and identified two broad approaches (UK Evaluation Forum 2006). The first focussed on measurable research impacts, using bibliometric methods, case studies, peer reviews, surveys and consultations. The second, broadly economic, approach used a number of methods to determine the value of research, including those seeking to assess direct savings generated to health care systems, to the economy and to society by successful translation. In their report, the Forum commented favourably on the 'Research Payback Model' which has been used by some funders, for example the Arthritis Research Campaign, to evaluate their funding strategies (Wooding et al. 2004). However it concluded that no one method on its own was particularly satisfactory, and that there were 'significant challenges facing those who were required to respond to demands from stakeholders' that medical research should demonstrate more effectively its social benefits.

From the point of view of social science, the repeated call for more effective measures of translation, and the aspiration to couple performance levels on these measures with resources, and hence to manage and rationalise the translation process, itself comprises a familiar turn in contemporary governance of institutions, and one that is often

somewhat ritualistic in character.. As the historian and analysts of accounting Michael Power asked, in his highly influential study of what he termed the 'audit explosion' (Power 1997:xii):

How and why did auditing become so attractive to so many diverse groups? Do all these audits have something in common? How do they work? How can auditing be such a robust policy tool when it often seems to fail so spectacularly? And how do we begin to understand a society which seems to invest so heavily in such an instrument of regulation? Is Britain becoming an 'audit society'?

How, we might similarly ask, has the translational imperative come to achieve such prominence in the governance of bioscience and biomedicine? Is translational accountability, of the kind envisaged by Cooksey, advocated by Ernst and Young, and now expected to be the first priority of the national research councils, part of a new 'Impact Society'? Will this imperative of translation, despite seeming so self-evidently desirable, come to fail as spectacularly as audit has in other areas?, Will the emphasis on accountability actually divert intellectual resources and research efforts away from those very activities which actually do lead to improvements in health outcomes? Alternatively, might an increased awareness of the extent to which 'the translation question' is linked to this more general audit explosion, and share some of its characteristic features, enable us to attempt to pose this question differently? If the attempts to measure translational outcomes have become, in Power's terms, 'rituals of verification', part of what sociologist Charis Thompson (2007) has called the 'promissory economy' of bioscience and biomedicine, how might one avoid the enhanced emphasis on the public benefits of biomedical research itself becoming 'translated' into an array of rhetorics and rituals of translation, reinforcing the very situation it is intended to disrupt?

Chapter One of this report briefly reviews the literature on translation and its evaluation drawing similar conclusions to the evaluation forum cited above, and social scientific research on the turn to accountability measures more widely, that despite the urgent need for evaluation, no ready made and unproblematic method exists by which

the MRC might capture the impact of its investment in research. Indeed, despite the alluring simplicity of the phrase “bench to bedside”, all those who work in this area, including Cooksey, realise that the process of translation is highly complex and far from linear.

These insights have been the basis for a number of reforms within the MRC to improve its translational strategy, and this report attempts to work in concert with these strategic efforts, while also attempting to suggest means by which the translation question might be reconsidered. Indeed, this process has already begun through the MRC’s own efforts. As translation has become an increasing priority within the MRC, so too have its models of translation changed. For example in the wake of the Mar Hall group review of scientific opportunities for health delivery, 10 key areas of translational opportunity were identified, and used to inform the development of the MRC strategic plan across its four boards. The MRC’s new strategic plan for 2009-2014, *Research Changes Lives*, is strongly orientated towards translation in all four of its strategic aims, but perhaps most strongly in the first two: 1) Setting research priorities which are most likely to deliver step changes in the potential for improved health outcomes, and 2) bringing the benefits from excellent research to all sections of society (MRC 2009). Both Research priorities themes under Strategic Aim 1, namely ‘Resilience, repair and replacement’, and ‘Living a long and healthy life’, are examples of the attempt to embed translational goals and deliverables into the identification of core research priorities, that is, at a primary stage of research governance. While consistent with the conventional, linear model of translation, by initiating translational efforts ‘further upstream’, strategic aims 1 and 2 can also be interpreted as a challenge to the linear model, insofar as they widen the range of possibilities of how translational outcomes can be measured, and also increase the number of variables that can be considered ‘translational’ – for example the participation of patient groups in new regenerative treatments.

In line with these reforms, as well as the findings of the Cooksey report, and other evaluations of translational efficacy, this report attempts to assist in the characterisation of the MRC translation process through a limited programme of basic research on the processes involved.

The current study

The current study seeks to assist in the evaluation of translational processes, by exploring how such an assessment can be made in a way that recognizes the complex dynamics, temporalities and meanings that structure relationships between investment in research and contributions to improved health and quality of life, as well as economic competitiveness. We use the term ‘health and wealth’ in this report to encapsulate such contributions, while recognizing, of course, that the definition and measurement of indicators of health and wealth’ remains a contested issue. We explore these questions, both in general, and through a specific case study of MRC investment in psychiatric and neuroscientific research at the Institute of Psychiatry (IoP), King’s College, University of London.

The principal objectives of the study are:

1. To undertake a critical assessment of existing methods of assessing medical and scientific outputs and their relevance to the generation of health and wealth’
2. Through a case study of a specific area of MRC funding, to clarify the evaluation criteria appropriate, or inappropriate, for an assessment of the contribution of such funding to health and wealth
3. On the basis of the above, to propose some ways in which analytically robust and empirically justifiable criteria for determining ‘value’ might be developed, in the context of MRC knowledge production both within and beyond health and wealth indicators’

4. To approach these questions not only through consideration of existing models of translation, but to attempt to widen these models to accommodate a broader range of factors influencing translational outcomes.

Background to our approach

Our approach to these objectives does not emerge out of an established sub-discipline of evaluation, but from the perspective of historical, social and anthropological studies of innovation in science and technology. It also comes from social studies of the emergence of the ideas of bioeconomy and biocapital, and their centrality in political support for investment in biomedical research: most European countries, including the UK, see such investment justified, in part, in relation to the idea of a knowledge-based bioeconomy, in which public investment in biomedical research generates paybacks by contributing both to improved health and to economic growth and development. From the perspective of these studies, we can see that the apparently simple question of linking investment to desired outputs in terms of knowledge, value and health becomes significantly more complicated. On the basis of our own research and that of others, we can list a number of challenges for such an evaluation

The timescale of scientific research

The timescale of scientific and biomedical discovery is often very different from the timescale of research investment. Research funded and undertaken today may not yield its benefits until many years down the line, sometimes twenty or thirty years later. Research which appears 'basic' and without possibility of translation today, may, when combined with other developments years later, suddenly generate outcomes. Indeed, many of the most valuable outcomes of scientific research have been neither planned nor expected. Research may be put into service in relation to problems that did not even exist or were not even conceptualized at the time the research was undertaken. Outputs in terms of health or wealth are seldom derived from one single source, type or sub-field of research: benefits are frequently, and increasingly, generated from the linking of research findings in different areas, together with

statistical and mathematical modelling and technical advances in visualization and measurement techniques, apparatus design and so forth. Each of these areas will have different temporalities and development may be spread over time and space, in many laboratories, funded in many different ways, such that it may be difficult to identify the contribution of any one piece of research or source of investment to the practical outcome. The contribution of research to health and wealth' may be contained in the knowledge pool' itself, rather than in any distinct element within it.

The diversity of criteria to judge value: value for whom?

As many of those who conduct economic evaluations are aware, different stakeholders may use different criteria to judge whether or not research has had positive economic benefits. A health service, for instance, may legitimately value innovations which reduce costs, while patients may value innovations which enhance their sense of being 'treated well' whatever the cost. Innovations which generate value of one sort, in the field of health, may actually be drains on value of another sort, in terms of economic criteria. For example, advances which enable very premature neonates to survive are very expensive for health services, and may not pass a population-based cost-benefit evaluation; and yet, for parents involved, they contribute to the inestimable value of a living child. In vitro fertilization generates inestimable value for parents seeking to reproduce but is extremely costly to health services. There are many similar examples.

Many evaluations of contributions to health and wealth are also controversial and contested. For example recent proposals to shift the emphasis of first line treatment of mild to moderate psychiatric disorders in the NHS from psychopharmaceuticals to cognitive behavioural therapy (CBT) derived some of its rationale from a cost-benefit analysis: the costs of the treatment were outweighed by the savings that would be generated by reducing the economic cost of mental disorder. These findings were based on generalization of studies of the efficacy of CBT, and might be thought to be an example of evidence based policy designed to maximize the health benefits of funding

of services. However this move is contested by those who consider that whatever the efficacy of CBT in symptom reduction, other forms of psychological therapy produce a different kind of improvement to quality of life through the kinds of insight generated by psychotherapeutic interventions. It also should be noted that this kind of evaluation sometimes elides some of the discrepancies between where the costs fall and where the benefits are accrued: while the costs accrue to those health services providing the treatment, the benefits include savings in multiple sites, for example, the costs of days lost through illness and of benefit payments

The context and role of evaluation in a 'knowledge based economy'

It is also important to recognise that the process of evaluation itself plays a key part in innovation and translation. The UK, like many other western countries, has come to consider itself a 'knowledge based' economy – and in this case a knowledge based bioeconomy. In such a context, knowledge is given a particular value, and this gives a specific character to knowledge as a form of capital in the bioeconomy. Thus we need to consider what, if anything, is distinctive about conceptions of biomedical research in the framework of a knowledge-based-bioeconomy, and the ways in which this shapes criteria of value and evaluation of such research. How, for example, do the standards and procedures for quality assurance and ethical oversight of human embryonic stem cell research developed by the UK Stem Cell Bank enhance the UK's standing in a highly competitive field? To what extent will the UK stem cell banking initiative contribute to the accumulation of health and wealth advantages within the UK, and internationally, in years to come? How can innovative models of public-private partnership facilitate the growth of this sector at a crucial stage in its step-change toward widespread applications for conditions such as juvenile diabetes, macular degeneration, or spinal cord injury? We need to investigate the different values accorded to knowledge in this context, and in particular the ways in which the different stakeholders involved accord different and perhaps incompatible values to different forms of knowledge. Those researching in this area need to attend to the core

values in exercises of evaluation: how are these values derived, what model of scientific progress do they embody, and to whom are they important? Most fundamentally, how is successful innovation in terms of health and wealth deliverables defined?

The Role of the Translational Imperative in a Post-Audit Society

If translation is, as one of the interviewees for this project described it, 'something that is handed to researchers from the outside and has to be made sense of', where did it come from? Who handed it over, and why? In his influential analysis of the ways in which auditing practices become an entrenched component of contemporary governmentality, Michael Power explains how such practices not only manifest themselves in new procedures imagined to enhance public accountability for 'relatively autonomous' groups of professionals such as doctors, teachers, or researchers, but also how such procedures themselves in turn 'create new mentalities, new incentives and perceptions of significance' (Power 1997:97). The 'mentality' of the audit society, Power argues, is most appealing when such measures are viewed as beneficial sources of organisational change. Their 'fatal flaw', however, is that the desire to rationalise by imposing or encouraging a single logic of accountability overlooks the actual plurality of logics at work in any single organisation. As he writes (1997:97-98):

auditing is explicitly a vehicle for organisational change...but it is rarely successful...for a number of reasons. The institutional environment of organisations is not usually homogenous and consistent. Different institutional logics of evaluation exist. Financial and non-financial conceptions of performance live uneasily side by side...In addition, different professionals articulate competing claims to problem solving.

This tensions not only disrupt the smooth functioning of the auditing process, but may, according to Power's analysis, lead to the opposite of what is intended by creating forms of dysfunction for the audited service itself.

Like Power, other social scientists have emphasised the relationship of auditing practices not only to externally-imposed monitoring, but to forms of self-monitoring that may reshape individual practices and definitions of value (Rose 1999, Strathern 2000). The recent debates about the potentially deleterious impact of impact measures on UK science are a manifestation of the concerns that have been expressed elsewhere about the connection of the imperatives of audit, impact and accountability to an enterprise culture. In this context, the translational imperative must be viewed as a double-edged sword. On the one hand, it is clearly important if the goal is to encourage scientific researchers to make their findings more useful. But on the other hand, social scientific and organisational management research has shown that accountability techniques can, in practice, turn out to be counterproductive tools to achieve these ends.

Choice of case study

A case study approach was chosen for the purposes of this report in order to address the question of translation from within a single organisational culture. The case study approach is particularly suited to areas where there is little prior knowledge, and where the principal questions are about processes: "when 'how' or 'why' questions are being posed, when the investigator has little control over events, and when the focus is on a contemporary phenomenon with some real-life context." (Yin, 1989: 13). We therefore consider that it is a highly appropriate method, therefore, for addressing the questions described above. This is also so, we suggest, because translation is highly domain-specific: the issues of translation in one field, say psychiatry – where the relations between basic neurobiological research and clinical applications are problematic and contested, are rather different from those in another, such as cancer – where there have been clear advances in relating basic biomedical research on pathology to clinical applications. A case study approach is also appropriate, we

believe, because questions of translation are less clear in relatively new fields such as neuroscience and the study of gene-environment interaction: there is less history to such fields to enable us to find points of comparison, and the nature of the field itself is still fluid (Abi-Rached and Rose 2009).

Following discussion with the MRC, it was agreed that the focus should be on the area of neuroscience, and it was decided to base the case study on the Institute of Psychiatry (IoP), which has been part of King's College, University of London since 1997. The IoP is the UK's leading research and training institute for basic and applied research in neuroscience, psychiatry and mental health services. The MRC has long been a major funder of research at the IoP, funding individual research fellows, research projects and programmes, and a number of research centres. Our research concentrates on one centre, the SGDP, which was launched in 1994 as a partnership between the MRC and the IoP.

The SGDP itself grew out of a sequence of MRC funding dating back to 1948, and its history was charted by the current Director, Professor Peter McGuffin, writing with Robert Plomin, to mark its tenth anniversary (McGuffin and Plomin 2004). As McGuffin and Plomin document, Aubrey Lewis was appointed in 1948 as the director of the first MRC unit at the Institute of Psychiatry, the Social Psychiatry Research Unit. Michael Rutter, who had worked within that unit, became director of a new MRC funded Child Psychiatry Unit in 1984. In 1993, according to McGuffin and Plomin, the MRC decided to close the Social and Community Psychiatry Unit (as it had then been named) but it did not seem either to the MRC or to the Institute a correct decision to abandon social psychiatry entirely after more than 45 years of influential research. The outcome of subsequent discussions was a successful bid from Rutter and David Goldberg, then head of the Institute's Department of Psychiatry, for an MRC programme grant to provide core infrastructure support for a centre, under Rutter's directorship, that would link neurodevelopmental research and social psychiatry with

the newly reenergized field of psychiatric genetics: this was the SGDP Centre. Today the SGDP describes itself as a unique multi-disciplinary institution that studies social epidemiology, child and adult psychiatry, developmental psychopathology, development in the family, personality traits, cognitive abilities, statistical genetics, and molecular genetics.²

In fact, the choice of the SGDP proved fortuitous, not least because the Centre has itself been undertaking work on translation, having a number of workshops on the issue, and with two of its senior academics, Michael Rutter and Robert Plomin, having drafted a paper on translation: Pathways from science findings to health benefits, circulated to SGDP colleagues in 2008 (now published as Rutter and Plomin 2009). We discuss these activities in a later chapter, but they serve to indicate that questions of translation - what it is, how it should be prioritised, what it might mean in practice and so forth – are not merely external to the work of researchers – they are becoming important, but in different ways which we hope to explore, to the development of research pathways, the writing of grant proposals, the presentation of results and to the internal culture of research centres and institutes in the life sciences.

Data gathered

There are four components to the research.

Literature on translational research

The first component is a literature review of materials about translational research, including the history of the concept; different models of translation and their relationship to models of scientific knowledge development and of research diffusion; methods used to evaluate translation. The results of the literature review are presented in Chapter 2 of this report.

Interviews with stakeholders in biomedical translation

The second component, presented in Chapter 3, involved in-depth interviews with stakeholders in translational issues. The stakeholder interviews were intended to establish the views of external parties who had their own perspectives on translational issues, and also as an initial orientation to establish the main lines of questioning for the subsequent interviews with researchers. A total of eight stakeholder interviews were carried out: three with members of the MRC, one with a clinician, two with senior figures working at the IOP, one who could provide an industry perspective on translation, and one with a professional research translator.

Interviews with researchers at the IoP

The third component of the research, presented in Chapter 4, was a series of interviews with researchers at the IoP. Following the literature review and the stakeholder interviews and the literature review, a topic guide was drawn up (Appendix One), designed to structure the in-depth interviewing. The topic guide was organized around three areas: how individuals saw the values that motivated their research, the importance of collaboration and interdisciplinarity, and finally their understanding of translational research and their views of it. Prospective interviewees were chosen on several criteria: that the sample would reflect the range of research interests of the Centre, that researchers holding MRC funding would be represented, and that researchers at all levels of seniority would be interviewed. A total of thirteen researchers in the Centre were interviewed. Each interview lasted for, on average, about one hour.

Bibliometric analysis

The fourth component of the research is a bibliometric analysis of research outputs of the centre. The results are presented in Chapter 5. For this, data was gathered from a variety of sources:

- The Science Citation Index (SCI) and Social Science Citation Index (SSCI) for peer-reviewed publications
- The Nexis News database for reports in mainstream publications such as broadsheets and publications such as the Economist.
- Materials gathered from searches on the House of Parliament publications website for appearances of members of the SGDP in committees.

2. TRANSLATIONAL RESEARCH: HISTORY, MODELS, AND METHODS OF EVALUATION

Pasteur: “To the individual who devotes his or her life to science, nothing can give more happiness than when the results immediately find practical application. There are not two sciences. There is science and the application of science and these two are linked as the fruit is to the tree.”

(quoted from Hait 2005: 4275)

William Hait, reporting on the deliberations of the American Association for Cancer Research in 2005, remarked that “Translational research is difficult to define but recognizable to all who engage in it.” (Hait 2005: 4275) . The burgeoning of this term over the last decade, and its movement from more obviously ‘applied’ areas such as cancer research to coverage of all forms of basic and applied research means that it presents itself to researchers as a *fait accompli*.³ Yet it seems that many practising researchers, while recognising the current salience of the term, find it a somewhat ‘slippery idea’. At the SGDP, for example, two stakeholder interviewees talked about meetings that they had held to puzzle over what it might mean for them, leading to a paper with their own interpretation of the “translational” in translational research (Rutter and Plomin 2009). We discuss the SGDP debates on translational research in Chapter 4. But how has the language of translation come to permeate the activities of biomedical researchers in so many regions of the world.⁴

There have been many histories of the idea of translational research in science, and here we will provide only the briefest of outlines.⁵ References go back to Francis Bacon and the 17th Century, passing through iconic figures such as Pasteur, and the quadrant of ‘pure basic’, ‘pure applied’, ‘curiosity driven’ and ‘use inspired’ research which was attributed to him by Donald Stokes (Stokes 1997). The modern history is usually traced to Vannevar Bush, and the view he expressed in the wake of the

experience of the Second World War in *Science: The Endless Frontier* (Bush 1945) that the US needed to build its own science base in the post war era. His first recommendation was that “Science, by itself, provides no panacea for individual, social, and economic ills. It can be effective in the national welfare only as a member of a team, whether the conditions be peace or war. But without scientific progress no amount of achievement in other directions can insure our health, prosperity, and security as a nation in the modern world”, and he is commonly believed to have argued that the principal justification for government investment in basic science was to generate those applications - “It is clear that if we are to maintain the progress in medicine which has marked the last 25 years, the Government should extend financial support to basic medical research”. This report led to the establishment of the National Science Foundation in 1950, whose mission was “To promote the progress of science; to advance the national health, prosperity and welfare; to secure the national defense; and for other purposes” (NSF 2008 quoted from Maienschein et al. 2008: 45):

The social contract implicit in this act was clear: the public would invest in science, and they would get results to make their lives better. The scientific contract was clear, too: give scientists money to do the basic science that they wished to pursue in their decentralized, independent laboratories spread across the country, and they would produce important results with widespread implications. While their research would be judged by standards within science, the assumption was that the enterprise as a whole would produce publicly useful outcomes.

The period from the 1960s to the 1990s was one of conflicting developments in this area. On the one hand there were increasing criticisms of big science, and we saw the rise of critical movements challenging the role of science in the military, nuclear power, recombinant DNA (Asilomar), criticisms of the harmful effects of pesticides and so forth. On the other hand, in the US, the Bayh Dole Act was passed with the explicit aim of encouraging closer links between research in universities and industry, and making technology transfer easier, encouraging the growth of public-private partnerships in order to bring results of scientific research into practice, and, in the UK,

an emphasis on user involvement in research evaluation and the need for those applying for research funding to stress and claim benefits to user communities.

In the field of biomedicine, the 1980s and 1990s were periods of major investment by public bodies in both the US and the UK, replete with assurances from the proponents, and injunctions from politicians and research funders, that this investment must, and would deliver benefits for those outside the scientific establishment. Two major programmes were of specific relevance to the question of translation that we address here. The first, the Human Genome Project, entailed a US investment of \$2.7 billion in FY 1991 dollars, together with over £200 million from the Wellcome Trust, and the involvement of a large number of researchers and laboratories, in the endeavour to sequence the human genome. The details need not concern us here, but what is relevant were the translational hopes that were constantly referred to in debates about the project. Thus, Francis Collins repeatedly referred to the sequencing of the human genome in terms of its potential to bring about a revolution in medical practice in the twenty first century (Collins and Galas 1993; Collins et al. 1998), a theme that was echoed far and wide, from public bodies, through researchers in grant applications, introductions and conclusions to papers and press releases, and in the market reports of commercial companies. Leroy Hood writing in 1992 under the title 'Biology and Medicine in the Twenty First Century, in the book he co-edited - *The Code of Codes* – believed that, “Once the 100,000 human genes have been identified” it would transform our ways of dealing with human diseases (Hood 1992: 155-157):

The genome project in the twenty-first century will have a profound impact on medicine, both for diagnosis and therapy ... Perhaps the most important area of DNA diagnostics will be the identification of genes that predispose individuals to disease. However, many such diseases – cardiovascular, neurological, autoimmune – are polygenic; they are the result of the action of two or more genes. Human genetic mapping will permit the identification of specific predisposing genes and DNA diagnostics will facilitate their analysis in many different individuals ... Perhaps in twenty years [he was writing in 1992] it will be possible to take DNA from newborns and analyze fifty or more genes for the allelic forms that can predispose the infant to many common diseases... For each defective gene there will

be therapeutic regimens that will circumvent the limitations of the defective gene. Thus medicine will move from a reactive mode ... to a preventive mode. Preventive medicine should enable most individuals to live a normal, healthy, and intellectually alert life without disease.

This rhetoric of translation of basic science to clinical applications, with revolutionary consequences, persists through arguments for the projects that succeeded the original HGP, notably the HapMap and Genome Wide Association Studies – with now the added claim that the medicine of the 21st Century will be personalized, predictive and preventive.⁶

Similar claims, although perhaps more moderate, were also made at the time of the increased investment in research in basic neuroscience that was, in the US, termed 'the decade of the brain' – indeed George H. Bush's 1990 announcement of this programme of research is replete with hopes that:⁷

new era of discovery is dawning in brain research. Powerful microscopes, major strides in the study of genetics, and advances in brain imaging devices are giving physicians and scientists ever greater insight into the brain. Neuroscientists are mapping the brain's biochemical circuitry, which may help produce more effective drugs for alleviating the suffering of those who have Alzheimer's or Parkinson's disease. By studying how the brain's cells and chemicals develop, interact, and communicate with the rest of the body, investigators are also developing improved treatments for people incapacitated by spinal cord injuries, depressive disorders, and epileptic seizures. Breakthroughs in molecular genetics show great promise of yielding methods to treat and prevent Huntington's disease, the muscular dystrophies, and other life-threatening disorders.

Something like a linear model of translation was implicit in these hopes. While the problems would be set in the clinic, the results of basic research would provide the means to answer them, and thus clinical advances would be tied to, dependent upon, and advance in step with, advances in basic biological knowledge.⁸

Godin (2006: 639) summarizes this model thus:

“The model postulates that innovation starts with basic research, then adds applied research and development, and ends with production and diffusion:

Basic research → Applied research → Development → (Production and) Diffusion

In many ways, it has been the relative failure of this conception of translation, notably the failure of genomic medicine to live up to its promises, that seems to have inspired the current debate on translation. In the US, this was marked by Roadmap issued by Elias Zerhouni, Director of NIH, focusing heavily on translation of research in the life sciences into clinical practice, and embracing the linear model:⁹

Ideally, basic research discoveries are quickly transformed into drugs, treatments, or methods for prevention. Such translation lies at the very heart of NIH’s mission. Although NIH has historically been successful by funding medical research that has helped to transform once acute and lethal diseases into more chronic ones, it has become clear to the scientific community that our country will need to recast its entire system of clinical research if we are to remain as successful as in the past.

In the US, certain characteristics of the health care system have been seen as particular impediments to translation along these pathways, notably the resistance to clinical guidelines – or ‘consensus statements’ – by many doctors and ‘for-profit’ medical facilities.¹⁰ Nonetheless, a key addition to this linear model, in the current official pronouncements on the need for translation, has been the additional belief that translational processes will be enhanced and speeded up by the close involvement of end users, notably commercial companies, in the translational process, largely through encouraging closer ties between universities and those companies, via the establishment of technology transfer offices, encouraging licensing agreements for companies to bring discoveries made in the universities into production, through the translation pipeline, and the like.

As we have seen, in the UK, the imperative of translation has been given a canonical form, and institutional and economic shape and authority, by the Cooksey Review (Cooksey 2006). Two examples given in the Cooksey Review indicate what, from this perspective, an ideal translational narrative might look like [2, §2.4]:

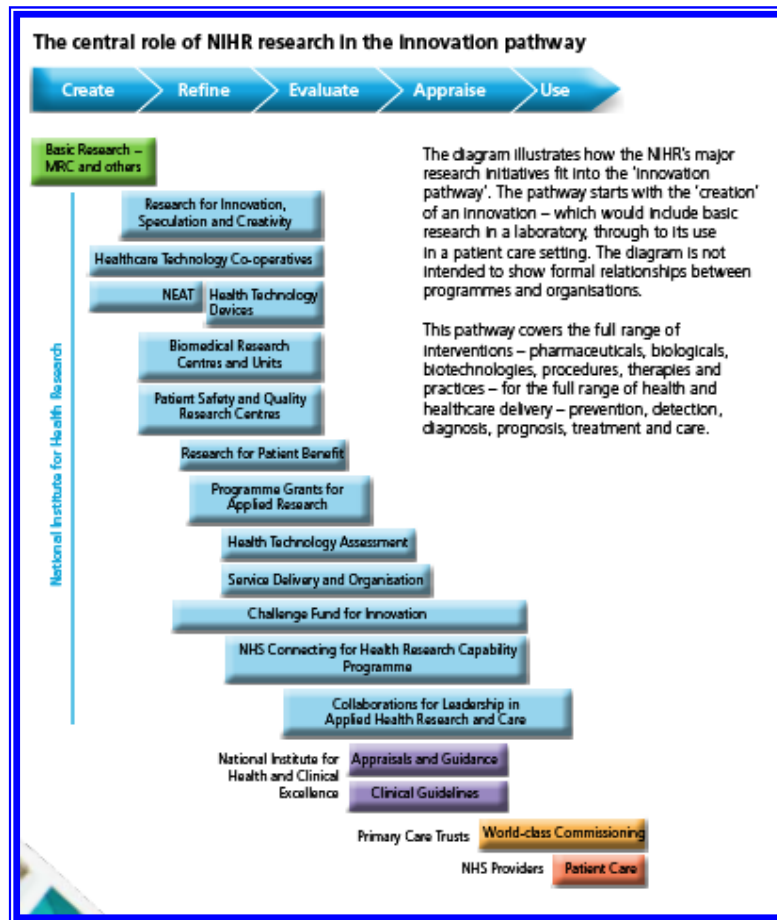
- At the University of Leicester, a team led by Alec Jeffreys used molecular biology techniques to study genetics variation in human DNA, resulting in the discovery of DNA fingerprinting in 1984. This has had a major impact in healthcare as well as society more widely. It has revolutionised genetic markers for disease and the way that organs available for transplantation are matched with patients, and it is also commonly used forensically in criminal investigations; and
- The isolation and reproduction of monoclonal antibodies in 1975 was originally developed by Dr Cesar Milstein and Dr George Kohler at the MRC Laboratory of Molecular Biology as a research tool to study the immune system.
- The production of therapeutic monoclonal antibodies has had a dramatic impact on biomedical research and on therapeutic products being developed to treat a variety of diseases, including cancer, asthma and arthritis. The MRC was paid over £100 million for its human monoclonal antibody Humira® last year.

Many scientists are critical of this model, because it does not capture the uncertainty inherent in basic research. Furthermore, there are stronger versions of this criticism that suggest that the Cooksey model is a 'treasury model' that has no connexion with the reality of basic research, and which places too great an emphasis on the translation of research into new drugs and too little on other kinds of research realization, such as policy change. These sorts of questions open up a space within the concept of translational research that may be studied sociologically as a kind of "discourse or rhetoric rather than as simply a normative attribute or fact of contemporary medical knowledge-production" (Wainwright et al. 2006: 2053). There is a sense in which translation, at the level of concept and indeed at the level of a noun phrase, may be seen as a category coming from outside of the life-world it describes, and the appropriate questions to ask of its usage in a given context are how well does it fit with actors' self-described activities: how do they "puzzle over" the concept and find some

rapprochement between, as one interviewee put it, “what we call translation and what they call translation?” This ‘translation gap’ is compounded by divergent models of translation *within* existing fields. For example, bringing products from ‘bench to bedside’ may be the reverse of the model used in NHS partnerships with private companies, such as those in the tissue engineering sector, who must bring their products from the bedside back to the bench – or rather to and fro in a classic product development feedback loop (Franklin and Kaftanzi 2009).

One response in the UK to these problems of translation was the establishment of the National Institute of Health Research (in 2006), whose aim, to quote its slogan, was that of “improving the health and wealth of the nation through research”.¹¹ The NIHR has undertaken a number of initiatives that bring together research from the Medical Research Council and the Department of Health, working with researchers and with industry with the aim of achieving better coordination of health research and more coherent funding arrangements, specifically in the name of translation. In the words of this report (NIHR 2008: 61).

One of the key points made in the Cooksey Review was the need to bridge the gap between basic scientific discoveries and new ways to prevent, diagnose and treat disease. To bridge this gap we are now working closely with the MRC under the umbrella of the newly established Office for Strategic Coordination of Health Research (OSCHR) Board to develop an integrated strategy for publicly funded health research.



The NIHR envisages its translational activities in terms of a complex array of activities, institutions, networks and flows of knowledge, as illustrated, for example in the above diagram of its 'innovation pathway' (NIHR 2008: 43). This, together with the recent innovations within the MRC itself, as set out in its Strategic Plan, suggests that a new and more complex, socially and institutionally aware, model of the dynamics of translational research is taking shape. It is, however, too early for a proper evaluation of the implications of these promising developments in conceptualising translation and seeking to promote it.

In the next chapter, we consider in more detail some of the views of the stakeholders in this debate over translation, as it relates to our own case study.

3. STAKEHOLDER VIEWS OF TRANSLATIONAL RESEARCH

The stakeholder interviews were intended to establish the views of some important external parties who had their own perspectives on translational issues, and also as an initial orientation to establish the main lines of questioning for the subsequent interviews with researchers. A total of eight stakeholders were interviewed: three with members of the MRC, one with a clinician, two with senior figures working at the IoP, one who could provide an industry perspective on translation, and one with a professional research translator. In addition, we were able to see an early draft of a paper written by two senior academics at the IoP who are both active researchers and institutional managers, Professor Sir Michael Rutter, a former director of the Institute, and Professor Robert Plomin, Director of the SGDP. on 'Pathways from science findings to health benefits', (now published as Rutter and Plomin 2009) which set out their views on the translation debate, and to some extent articulated an 'official position' for the Centre. We have drawn on this material in the present chapter.¹²

Examples of successful translation

Our stakeholder interviews generated a number of examples of what was thought of as 'successful' translational research following something like an 'alpha narrative' of the translational pathway: Basic research → Applied research → Development → Production → Application in the Clinic. The Laboratory of Molecular Biology, Cambridge (LMB) was cited by two interviewees as a prime example of successful translational research, principally on account of the isolation and reproduction of monoclonal antibodies there – an example also used by Cooksey. Why was this considered to be so successful? One of our interviewees cited its structure and way of

working – the size of the research groups that it employed (when a group gets larger than four or five, it is broken up). And, broadly, it was thought to be something to do with the way they work there. However, it is always important to be wary of post-hoc judgments (i.e., merely choosing this feature retrospectively as the key to translation, simply because the research came up with useful applications).

More generally, however, our stakeholders tended to be rather sceptical of this ‘alpha narrative’ of the way that translation works. Rutter and Plomin, in the paper we have already mentioned, select three examples that recurred in many of our interviews, each of which show something of the view of many stakeholders familiar with the research process about the complexities involved. Rutter and Plomin thus point out that the findings about the relations between smoking and adverse health outcomes emerged first in epidemiological studies in the 1950s, not from basic science. It took a decade of controversy, finally leading to animal studies showing the carcinogenic effects of the tars present in cigarette smoke, and, in 2004, to general agreement that there was a causal pathway from smoking to cancer, and only in 2007, to findings on the effects of gene expression. They write (Rutter and Plomin, 2009: 530):

First, this was an example in which the starting point did not come from basic science but, instead, epidemiological findings prompted the need for animal models and for studies of gene expression that took the matter further. Second, randomized controlled trials (RCTs) were clearly not feasible and hence, causation had to be tested in humans using observational data. That meant that rigorous crucial studies seriously considering non-causal interpretations were essential, and these were carried out. Third, the health benefits from eliminating smoking mainly had implications at a population level rather than at a patient treatment level. In other words health benefits need to be viewed in public health terms as much as in individual patient treatment terms ... Fourth, it took some 50 years to proceed down the pathway from the original findings to health benefit actions. Fifth, the progress came through a combination of research strategies that involved an iterative Interplay between observational studies and basic science and back again.

These were themes that they reiterated in their stakeholder interviews with us – that there was no simple path from bench to bedside but often a convoluted interplay beginning with epidemiological or clinical findings; that the timescale was long and

many different pieces of research were involved; that many of the benefits were to public health, and not confined to individual clinical outcomes, and that many different research strategies interacted.¹³ Rutter and Plomin reinforce this view with their example of the effects of lipids in predisposing to coronary heart disease – here basic research with rabbits in the early decades of the twentieth century was ignored, but experimental work on lipids in the blood in the 1940s and 1950s contributed to understanding of their role, and a longitudinal study in the 1950s showed that lipoprotein levels predicted later cardiac events. These led to further laboratory and animal studies, a further decade of controversy, not resolved by further evidence from clinical observation and longitudinal studies. Finally, in the 1970s, there were more contributions from basic research, and the issue was only resolved, to the extent that it has been, by the development of the statins which enabled RCTs (Rutter and Plomin, 2009: 531):

the pathway extended over nine decades and progress came in a series of steps bringing together the crucial non-experimental epidemiological evidence, experimental animal studies, genetic evidence, clinical observations, and clinical trial data. It was also important that the basic science provided key evidence on the biological mediation, but it was the non-experimental epidemiological data that prompted basic science, not the other way around. In this case, unlike the smoking story, the main benefits might be viewed in terms of the treatment of individual patients rather than public health considerations, but the latter are crucial in terms of prevention policies.

Rutter and Plomin's emphasis on the distinction between individual patient benefits and public health considerations may be overdone, but it is important to their own perception of the problems in the translational imperative. Their final example, that of fetal alcohol syndrome, was referred to by several of our stakeholder interviewees, to demonstrate a theme that is sometimes thought of as serendipity though often in fact depends on good clinical observation – accidental discoveries many years ago at the 'bedside' – in this case of malformations in the offspring of chronic alcoholic mothers – that became translated back to the bench, via studies in mice, later extended to suggest that what was involved was a process in which developmental exposure to alcohol reprogrammes genetic networks. More generally, this points to an interesting

valuation of naturalness in scientific work: for those who think like this, research is a particular 'ecosystem', and the consequences of interfering in its natural processes are uncertain. For some stakeholders, such narratives of serendipity, created and fostered by happy accidents and an environment supportive of creativity and freedom to explore multiple paths of interest, demonstrated the error of seeking to strategise translation. For others it was a negative example of researchers' resistance to the priority of translation, a perception that scientists are strategy-averse and that trying to make scientists have strategies is "like herding cats" because the narratives by which they work are episodic, they think of research in terms of particular stories where a minute focus on one thing by a specific individual or group leads to another development, often in another context and by other researchers, and so on until one reaches the moment of when application becomes possible.

For Rutter and Plomin, however, these examples not only show that the direction of pathways is as often from clinical studies to basic science, and the long time frames involved, but also that benefits are not so much to individuals as to public health. The key feature of what Rutter and Plomin term "experimental medicine" – and the key to translation, they believe, is not the clinical trial, but hypothesis testing, often involving "an iterative approach that takes a human observation between some environmental factor and disease as its starting point, goes on to test for environmental mediation, and then possible biological pathways for that mediation, proceeding next to animal models to examine these experimentally, and then returning to the human situation to determine whether the mechanisms apply to human disease." (Rutter and Plomin, 2009: 531-2). And, in the remainder of their paper, they seek to support this view with reference to the pathways to progress in the neurosciences, in genomics, in brain plasticity, in psychopharmacology, in social and cognitive neuroscience and in memory. While identifying some key areas of research that may have relatively swift clinical applications – epigenesis and the role of maternal and other environmental inputs; dementia and the discovery of neurofibrillary plaques and tangles, and drug

dependence, they argue that in most cases it will be difficult if not impossible to judge what clinical applications might follow from basic research, that translational benefits may be placed most at risk by an “ill-considered rush” from laboratory findings to randomised controlled trials to adjudicate efficacy, and that what is required is carefully considered hypothesis-based bridging research, located in the context of two-way transactions, to determine whether, and how, research findings may have clinical or public health implications.

The culture of basic science

One theme that appears frequently in the stakeholder interviews is the belief that there is some kind of fundamental tension between the cultures and practices of basic scientists and that of clinicians and clinical researchers. From some perspectives, basic scientists are characterized as actors who look no further forward or back than their next piece of research and their next publication and are neither interested nor amenable to an agreed or articulated developmental strategy. Thus, one of the issues that emerged at an MRC workshop on translational research, held in response to the Cooksey Review, was the need for “cultural change within the research community and recognition that translating research findings and communicating findings to research users was part of a researcher’s role” (Medical Research Council 2007: 2).

One aspect of this is the perception that there is a lack of understanding between those working at the bench and those at the bedside, a perception that has also been articulated in other social science research on translation (Wainwright et al. 2006: 2063):

Bench-to-bedside efforts have frequently been limited because clinicians often poorly understand the scientific aspects of laboratory science, while biomedical scientists can lack understanding on the problems of research with humans.

In a similar vein, one stakeholder suggested that basic scientists lack sufficient grasp of the statistics required to apply their results to human populations:

Our community has got the methods. Basic scientists often don't have methods, bless them. So things like statistical powering or study design are often problems. Until recently they often didn't address these properly, and there would be studies proposed that were badly designed and not properly powered, which just wouldn't get the results that they want: to fund these would be to waste money. More recently, they've improved their game, and realise that now you must have proper statistics. And the MRC has now set up a methodology panel to address this, and interestingly this actually comes under the translational medicine board.

From the perspective of our MRC interviewees, this can be seen in terms of a problem of how to encourage basic scientists to understand the idea of translation, and in particular the ways in which the funding of research should be linked to an assessment of methodological and other criteria that can locate that research within an articulated translational pathway – something which is not adequately appreciated by the basic researchers.

Research vs. advocacy

In contrast to these rather negative views of the translational efforts of basic researchers, several exemplars of translational scientists were invoked. As we have already mentioned, Richard Doll's work on the connexion between smoking and lung cancer appeared frequently in our interviews:

We need to think about what we're talking about when we talk about translation. [example Clinical Trials Services Unit in Oxford] Richard Doll has had a huge translational success [link between smoking and cancer], he could have left it at that, but he goes out there, he's like a prophet, he bangs on people's doors, etc.

[interviewer] I'm thinking that's a bit of a waste: someone else could have done the marketing, so to speak, and he could have gone on to discover something else.

That's a very interesting area actually. When I talk about getting people to change their attitudes I talk about persuasiveness, credibility and salience. Having someone like Richard means he is credible because he's an expert, whereas a market person doesn't have that credibility.

[interviewer] Is that part of a different problem: public understanding of science?

I'm talking about opinion-formers rather than the general public. He's implementing his research by translating his findings into a utility.

The image of the scientist taking on an advocacy or campaigning role is one example of a broader notion of translatable utilities from research. These are generally described as coming from the particular 'vision' of an individual or group:

Scientists think about translational research as moving a discovery along: 'that's really interesting, how can I move this along'. They don't see the endpoint as we're going to make a new widget or we're going to find the next statin.

A good example is monoclonal antibodies. That discovery wasn't made because they were looking for a great therapeutic target. But somebody had the vision that there could be a use for it, and that's what drove Greg Winter to humanize antibodies. And now that's an example of translational research that has an impact. But Greg wasn't doing that to create a specific drug.

The 'tunnel vision' of the scientist is contrasted, not only with particular individuals' 'vision', but also with drug companies, who have a commercial interest in the promoting of new drugs through advocacy:

A good thing to be thinking about: drug companies target opinion leaders to recruit patients because they want to engage the clinicians so that if the study proves effective ... the clinicians become advocates. So the drug companies plan how to take the product into the community. Basic scientists don't do that. They don't look at how the product of what they're researching is going to be taken forward. Scientists do something that they think is interesting and they just let it drift. We don't go to all the key people and say hey look at this, can you take my discovery beyond please?

[interviewer] *why is that then?*

Some scientists are only in it for the discovery. Rather than say how can we take this forward, they just go on to discover the next thing. When molecular biology was in its heyday, people kept cloning receptors left, right and centre, and they just kept on cloning receptors rather than understanding how the receptors function, their role in disease, screening disease-models to see whether these clones were there. It's only now that they're starting to do that. It was almost getting into the stamp-collecting mode. Only the really visionary ones were saying how can we take this forward?

Within the SGDP one may find a similar contrast between ‘just wanting to know’ and ‘taking this forward’:

Some of [the Centre’s research] is very basic, but some is very applied. Some programs, such as X’s, are planned with an end-goal of developing new interventions. As opposed to others such as Y’s, which essentially just want to know what the genes are. X could have just said well I’m just interested in what the cognitive deficits are, you could just mine that down and down.

And then you’ve got Z’s work which shows how an intervention might modify a predicted outcome. But even so, all Z is doing there is...not doing the science developing an intervention, but just identifying a risk factor and someone else can go off and develop it from there.

Here, there are two different kinds of translation-as-moving-along, the one aiming for the development of treatments, the other priming the ground for others to do so. This prompts the question whether in some degree translation is a sort of rhetorical figuring of research; could, for example, the characterization of Y’s work above be rewritten so that it is still accurate but also more ‘translational’?

This sort of question sits well with the MRC’s recognition at its 2007 translational research workshop that the need for cultural change should be accompanied with “guidance on the process of translation and an accompanying vocabulary to describe more precisely translational activities” (Medical Research Council 2007: 2). Thus, one possibly rewarding way of conceptualizing how ‘making translation happen’ may happen in the research setting is as a set of idiomatic definitions of research situations: where and how does research become framed as translational? is there a translational or counter-translational disposition? how many situations are produced within which translation could happen?

Beyond the metaphor of barriers

Our stakeholder interviews suggested to us the importance of resisting thinking of translational research as a 'path' and problems with translation as 'barriers'. Casting the process in this way involves making too many assumptions about the nature of translation, most particularly that there is a single path from basic research to clinical outcomes. Nothing in the data from the stakeholder interviews nor from papers on translation indicates that this is the case. There may not even be only a few relatively constrained paths to translation; indeed, it is possible that there may be as many different kinds of translation as there are fields.

This topic of the adequacy of the barrier metaphor came up in discussions with the MRC about what they would consider a good outcome of the current research:

The work on values needs to move us forward. Studies haven't been powerful enough: "barriers", communication skills, etc. What's going to take us forward from that, that's what we've got to get to. ... It could provide marvellous case studies, it could be something more analytical, more useful at an executive level. Understand what happens, and also to better understand ways of behaviour that we'd like to see in scientists.

Thinking of 'what happens' in terms of barriers can result in, at best, an ad-hoc catalogue from which it would be difficult to generalize: it would not capture the full specificity of the behaviour of scientists because it would always be organized around the normative rift between 'what they do' and 'what we'd like them to do' and between 'what they say translation is' and 'what we say it is'.

One way of thinking differently about translation is to use more nuanced concepts of constraints and enablements: what structures and practices are there that constrain and enable researchers to approach their research in a translational mode? An obvious example of this would be the availability of funding specifically for translation of basic research such as the recent activity of the Research Translator at King's. And, indeed,

much translation seems, by the accounts of our interviewees, to result from 'following the money':

I think there's been a change in culture, which has been partly driven by funding agencies. And it's also partly a general feeling in science that, I've mentioned that geneticists have had a lot of money, and you've found a few things, but where is the use in that? And there's always the example that not a single pharmaceutical has been developed from genetics, at least not yet, anyway; I'm sure that will happen. So, there's been that, and there's been a push from organizations like the MRC to lead us down that route by having these funding schemes.

Conversely, there may be factors, historical, institutional, disciplinary and cultural, for example, that 'impede' or push the researcher away from the translational. Thus, one could think of the research setting as something similar to an electronic circuit: the problem of translation thought through in this way would be a problem of optimization: which arrangement of components, the equivalents of resistors, capacitors and transistors, produces the greatest translational effect given the inputs?

Conclusion

It seems clear that the rhetoric that forms the 'alpha narrative' of translation is that of a path following the linear model of scientific research and innovation, and the idea of a "translational superhighway" (Lenfant 2003: 869). And this rhetoric needs attending to for its impact on the researchers themselves. Does this rhetoric have any salience for them? And if so, how do they assimilate it into their practices?

One way of analysing the different positions taken up in our stakeholder interviews would be to think of the different places that the idea of translation occupies in the narratives that the actors use to give sense to their ways of working and their priorities, and their own sense of their identity within the research setting. The research setting would thus be one among a number of what some sociologists have termed 'economies of worth' (Boltanski and Thevenot 1991). The notion of an economy of

worth is intended to focus our attention on the critical and justificatory operations that people perform in their everyday lives and work, and the principles and criteria that they appeal to in order to rank, prioritise and justify their actions and their choices. In the present context, this would direct our analysis towards the different systems of worth within different practices (discovery, status, curing illness, etc.), the congruencies and differences among these 'economies of worth', and the ways in which actors enacted these in their work, and gave them meaning through the ways in which they speak about them, narrate their lives, and in so doing, shape them. This might give us more grip upon the actual ways in which we might re-configure the existing structures and narratives to optimize them in relation to the translational imperative.

In short, to examine such pathways, we propose a model that requires (1) viewing translational research within the 'economies of worth' of different participants, and their modes of justification of the worthiness of research; (2) exploring the ways in which the actors identify themselves as persons of particular sorts - such as 'the clinician', 'the basic scientist', 'the pharmaceutical developer'; and (3) exploring the ideas held by researchers of the 'translation situation', that is to say the way in which the practitioners come, in different ways, to adopt particular narrative accounts of research and its pathways and motives, to define particular types of research, or research projects or research findings as 'translation situations', and adopt, or reject, a disposition to produce 'translation situations' in the way in which they go about their research activities in practice.

We continue to explore these issues through our interviews with the researchers themselves, presented in the next Chapter.

4. TRANSLATION AT THE IOP

In 2004, Peter McGuffin, then Dean of the IoP and a former Director of the SGDP, published two articles on the history of the SGDP, one written with Robert Plomin, currently the Director of the SGDP, and one written with Michael Rutter, who was the key figure (with David Goldberg) in negotiating with the MRC to establish the Centre (McGuffin and Plomin 2004; McGuffin and Rutter, 2004). In neither article is the issue of translation of the research into clinical or practical applications mentioned as a priority, although it is noted in passing. According to these histories, the rationale of the IOP was to overcome the long history of hostility between genetic researchers and social psychiatrists, by establishing an “an interdisciplinary research centre that could, in a comprehensive way, study the interplay of nature and nurture in the development of common psychiatric symptoms and disorders” (McGuffin and Plomin 2004: 280). According to McGuffin and Plomin, the focus of the Centre’s work was (McGuffin and Plomin 2004: 281):

on common psychiatric disorders, covering three domains: mood disorders (especially anxiety and depression), ‘externalising’ disorders (especially disruptive behaviour including hyperactivity) and cognitive disorders (especially language disorders and mild learning disability, including autistic symptoms). The Centre concentrates on the aetiological aspects – developmental as well as genetic and environmental origins – of behavioural disorders. However, there is a strong emphasis on methods of measurement and classification and an attempt to foresee the practical, clinical and public health implications of the Centre’s findings..

And, summarising the overall goal of the SGDP, Rutter and McGuffin write:

“Ultimately, the aim is that the Centre’s unique contribution will be the provision of an understanding of how genes work at the behavioural level in relation to the developmental interplay between genes and environment – a field that has been termed ‘behavioural genomics.’ Perhaps these authors merely took the translational issue for granted, and felt it covered by passing mentions. Be that as it may, within a

few years, translation was to become a rather explicit element in the internal discussions in the SGDP.

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We have already referred to the 2008 paper by Rutter and Plomin in which they contrast the importance of scientific research being seen to be 'useful' with the impossibility of determining such a path from the outset (Rutter and Plomin, 2009: 529):

The underlying notion is that science must expect to be judged on whether, over the course of time, it proves to be useful. So far as biomedical research is concerned, usefulness would ordinarily be defined in terms of individual health benefits. That is entirely reasonable, provided that there is a realization that the benefits of basic science are rarely apparent at the time, and that there is usually quite a long time-span between the original basic science findings and their practical application ... The idea that that potential can be assessed at the time of the funding of most basic science is fundamentally mistaken. In addition, however, there is a danger that translational research may be defined in ways that run counter to what actually happens in proceeding from scientific findings to health benefits.

For Rutter and Plomin, then, while health benefits are a laudable goal, there is no satisfactory way of measuring the translational potential of a piece of research until after the potential of the research has been realized, but that, importantly, it is not usually very clear when 'before' and 'after' happen.

In an interview for this study Rutter forcibly amplified his hostility to the 'daft and immoral' over-emphasis of the economic benefits of 'translation':

I am utterly opposed, lock, stock and barrel, to the notion of looking at the economic benefits of research. I think that is just daft and immoral.... The bringing of economic benefits seems to me a really damaging distraction. I don't care whether profits are made on something. I do care that it has benefits to the nation in terms of health. If you're improving health, there will, of course, be economic benefits that follow. So I'm not saying that the two are totally disconnected, but the way of asking, is this going to lead to patents that are going to bring in profit to the institution, I am utterly opposed to.

For Rutter, the equation of value with profitability represents a false economy, and more specifically a false lead. While a relationship between good science and health benefits clearly exists, and such relationships may lead to profitable markets, the assumption research can be directed to deliver this outcome is 'a damaging distraction'.

This view, as noted earlier, represents the strongest position of opposition to the translational ethos, not only rejecting its basic premises, but arguing they are false, costly, and misleading. But how widespread is this position, and what are its alternatives? In the remainder of this chapter a range of views of translation are presented and discussed.

What is translation?

Many interviewees had given some thought, no doubt stimulated both by the external environment and internal IoP discussions, as to the meaning of the term 'translation'. One interviewee stated his view of this process, and the challenges for psychiatric genetics, thus:

I think it's taking any form of research and turning that into something that's beneficial to society or an individual. So, in terms of genetics, that might mean that you take a basic genetic association, and then you turn that into a clinically useful test that could predict whether someone is going to get ill, or predict the course of their illness, or help determine which kind of drug or treatment they should have. So, that would be a direct translation, and I think in terms of genetics, that genetics hasn't really got to that stage yet, for common diseases. So, I've just come back from a meeting where we've done some big projects on schizophrenia genetics, and we've found chromosomal deletions that occur in patients that confer quite a high risk, so perhaps a 15-fold risk of developing schizophrenia. But they're very rare, perhaps one in 500 schizophrenic patients have this deletion, compared to one in 4,000, in the normal population. So, we're just trying to grapple with how we can translate that into something useful, in terms of developing a test on what the implications of that might be.

For others, however, this view that translation in some way covered all research that was in some way 'useful' - to clinicians or policy makers - was 'bland':

[there is] a very bland formula ... that translational research is useful research. I think that ... doesn't tell you anything. Presumably, if it's funded, it must be useful in some respect, so I don't think that is a useful formulation at all and I think it's a defensive formulation because of the fear that translational money, rather than being new money, is really diverting resources away from basic science and towards clinical trials. I've heard people say that any half decent clinical trial will get funded these days, because there's so much money sloshing around. So, there's a feeling that this is an attempt to persuade people to do clinical trials instead of basic research and because we're basic research here, that's a threat.

Another interviewee also referred to this bland notion of translation and some of its problems:

Yeah, what I understand is that it's the process of making basic research findings relevant to people who actually work with patients or at risk populations. If, for example, one is doing research in some sort of an animal model, it's the process of showing that the same mechanisms that are at work in the animal model are also at work in the human model; or, developing treatments based on more basic science that could be used in at risk populations.... I think, people have a very loose understanding of what translational research is, so you'll hear lots of people say, translational research is useful research. I think, possibly I have a sort of stricter definition of it than that, so, I think, many people here would say that a lot of what we do is translational research. Why would they say that? They would say that because it's research that's, for the most part, being conducted in human populations for example as opposed to in animal models of disease. It's research that's being conducted in epidemiological samples, as opposed to various clinical samples; so, I suppose, that's why people would say it.

Many of our researchers thought that the process was complicated, and it was very difficult to say what would be translated in research:

I think research is useful on lots of different levels; so, I think some people do research that has very immediate applications in a variety of settings, whether that's in health or in education or in social policy. I think a lot of science is just a very gradual accumulation of basic findings that at some point accumulate to inform practice because they finally latch on to some mechanism that can actually be used to develop a treatment of some sort, or can be used to inform the way an intervention is developed. And what exactly do you do with families that X, Y, Z could happen, so I have some faith that eventually there is an accumulation of these

findings and they matter; but it's not the sort of research that one can take away and translate immediately into some sort of policy in intervention.

But it was clear that some thought there were good examples of translational research in other areas of medicine. Thus one interviewee thought that cancer research was the best example of effective translation, along a straightforward pathway from bench to bedside:

There are a lot of different kinds of research that can ultimately lead to better medical care ... the obvious reference point here is the big cancer institutes that have been, now, running for a generation where very large amounts of money were made available through the specialised institutes, specifically directed to improve the treatment of cancer. And a large amount of that money went to studies that were focused rather narrowly on specific treatment and clinical goals, when the major breakthroughs came from basic science and understanding how cells grow and divide and thrive, and stem cell research. All the advances came out of very basic science, which were then successfully translated into clinical treatment. So, you've got these novel therapeutics, aimed at growth factors that are involved in providing blood supply to this [organ] ... people realised that humans have to have a blood supply and you cut off the blood supply this [organ] dies. That came very much out of basic research, nothing to do with clinical treatments. The clinical treatments came way after that. In fact, those kind of clinical treatments weren't even envisaged when those cancer centres [were set up], so I think that's instructive. [This is] one of the examples that people use to say that the goal is to translate basic science into clinical improvements, rather than to totally reorient the kind of science we do away from basic science and towards clinical science.

This interviewee, who had worked in the US in an institution expressly devoted to translational research, described this basic pathway thus:

At [specific institution in the US] that was the idea of what translational medicine was. It was about the idea that there is a progression from basic science through to clinical medicine that goes from understanding the underlying disease processes, identifying drug targets, validating those drug targets in vitro and then in animals and then in humans and then finally having a molecule that will influence that drug target and then testing that in a clinical trial, and then implementing it.

The same interviewee noted the resistance to the idea that could be found in some institutions:

in institutions like this, there is a good deal of resistance to the idea of translational medicine, for the very reason that it's viewed as potentially diverting research money away from the basic research that they think is [crucial]... I think, in this institution particularly, the thought process goes something like this: most of the advances that have come in health care in the twentieth century come from advances in public health. If you look at the increases in lifespan, they're all due to public health initiatives, and if you're talking about clinical efficacy, why is it that translational studies per se seem oriented [?] to new drugs when, if you think about what has increased the lifespan of the six billion people in the world, it's all about reducing infectious disease and providing clean water, stuff that the Bill Gates Foundation has done. I think there are definitely different ideas about what are the useful clinical goals and it depends very much who you are.

But he went on to argue that actually, many people did not realise that they were, in fact, doing translational research:

I don't think people here realise that they're already doing translational research.... I wouldn't really characterise the bulk of what I publish as being translational, in either spirit or intention. But, on the other hand, it's been cited ... in various contexts that can be called translational, in relation to clinical guidelines for treatment for specific disorders and stuff like that. So, I think genetic research does have application in various ways in informing clinical goals, even if it doesn't directly lead to improved clinical care, it informs what doctors do and what we know about disease, and I think that's useful and I think, in some sense, it's translational.

Another interviewee, who had actually become committed to the idea of translational research over her time at the IoP, and whose work on genetic susceptibilities and environmental triggers has been taken up in policy discussions in the UK and elsewhere, nonetheless expressed a criticism of the uses of the term in the current climate:

if I have any kind of criticism of the notion of translational research, it's that in order to get political will behind this translational movement, in order to get funding bodies to get serious about it, in order to get scientists serious about it, in order to get the public to believe in it, it's been necessary to focus quite narrowly on a

definition of translational research that really is randomised clinical trials or tertiary care, treatments for people who are already very ill, already need medication, already need a hospital bed so it's no accident that the phrase bench to bedside is used. The bedside implies that the place where research can make a translational difference is when the patient is already bedridden, right or in a hospital bed and being a longitudinal researcher who starts with children and follows them through life, I'm much more interested in prevention, the population level. So I think a lot of what happens here at the SGDP feeds into what could be conceptualised as translation, that is identifying key points in the life course where it would be most cost effective to intervene, identifying ways that social policy or public health policy could be shifted to prevent mental disorders starting in the first place.

She went on to give a specific example:

So just to give you a concrete example, if you were talking about translational research, bench to bedside translational research in addictions, mainly people would be thinking of can we develop new methadone maintenance type programmes for people who are already addiction patients. I think translation ought to include the possibility that we could intervene with teenagers at the point when they're first experimenting with drugs to prevent the pathway from initiation, experimentation, habit, addiction and relapse. The earlier you intervene, the cheaper and easier it ought to be but that kind of prevention approach doesn't seem to be brought into the translation.

She thus articulates a different idea of translation, and one that is more in line with the view expressed in the argument by Rutter and Plomin – that the key aspect of translation in psychiatry at least is not in individual treatment but in population level interventions for prevention, and policy interventions, not specifically psychiatric in nature, that may avert the triggering of a disorder, or may increase resilience to disorder.

Other researchers also thought that what was important was to influence social policy in a rather general way rather than to develop specific psychiatric therapies or interventions:

My take on translation from my own perspective is actually thinking about issues like getting policy makers to recognise that children have mental health problems that, probably 20 years ago they didn't. I think actually interestingly, just at the moment, there's a huge wave of interest in this kind of thing, which is sweeping off

in all kinds of directions.... But mainly my thoughts are, as I say, linking up with the policy community maybe and thinking how can we create a loop there that's going to be helping the 75% who don't get any attention..... [But] you also feel that the policy process is to an extent arbitrary and you can't control it in a tight sort of way. Everybody's keen on everything being evidence-based but there's a wave of that and then we move swiftly on to what we thought we were going to do anyway. And then try to find a bit of evidence to support it because the time frame is different and all of that sort of stuff. I don't spend a lot of time knocking on the door of X and Y myself. But I do spend time linking up with organisations that do that more, and in fact they also contact me, because they think it's useful to have somebody in the background that [knows] what they're talking about.

Thus we can see here that many of our interviewees at the SGDP, while they were extremely committed to their research having effects, saw those effects not in terms of translation to 'the bedside' – that is to say in the kinds of clinical applications that are normally thought of as arising from investment in medical research, but in terms of rather general policy transformations to reduce risks, increase resilience, and change the environments in which mental health problems may arise in the first place. This is, perhaps, an example of a rather general 'economy of worth' at the SGDP, and one that goes back to some of the early rationale for social psychiatry at the Institute of psychiatry. However those who took this view often recognised, that these kinds of translation effects are not only difficult to quantify but difficult to enact, given their reliance on rather slow changes brought about by social policies which are often shaped by other political and economic considerations and seldom 'evidence based'. They also depend on processes that are largely outwith the control or competence of biomedical researchers. Nonetheless, this way of construing translation, buttressed as it is by an appreciation of the ways in which many previous improvements in health have come about, is clearly important and often compelling.

Translation may threaten the importance of basic research at this stage in psychiatry

It was also clear, however, that some of our interviewees had ambivalent, if not downright hostile views of the current emphasis on translation especially as it applied to their particular area of research. A view expressed by a number of our interviewees, reiterating a point made by Rutter and Plomin, was that at this point of the development of psychiatry, as opposed to other areas of medicine, basic research was what was required.

One of our interviewees put it thus:

in psychiatry we know a whole lot less about these processes than we do in cancer ... Maybe, in psychiatry ...we're back in the 70's. We don't know what the important cellular or neurological processes are that are involved in disease. We just don't know what's going on in the brain, much as, six years ago, we didn't know what was going on with tumours. So, I think it's appropriate to use research money for basic research, because we simply aren't there yet. Once we've got to a certain point, once the basic science is known, then you have lots of jumping off points for clinical studies, and I think that in psychiatry we're not there yet.

And this was a particular issue for research in neuroscience, where much of the basic research is done with in model organisms and in animal models and the move to applications in humans is especially fraught with difficulties:

because we're focused on humans, you have to have the basic science reasonably well developed in order to conduct research into humans, because the scope has to be so much narrower. If you're looking at yeast, you can just dump everything in your cell and see what works. If you're in humans, there's both experimental and ethical constraints so I think we will get involved in that but it will be relatively late in the game, and you will have to have done initial studies to identify those biomarkers and make sure that they're important in disease processes.... There's a lot of different routes to the same goal. You can have very programmatic routes from basic science, in vitro, in vivo, and then to bedside in that very programmatic manner. That's something that we argue against here and I can point to lots of researchers who do the research the other way around, who use genetic research to identify risk factors for human disease and then take our understanding of

biological pathways gained from that research and then take it back into the cellular and animal models, to try and develop more broadly. So we get that ray of sunlight into those biological pathways, then we can take that back into the lab. So, to some extent we're going from humans back into the lab. And there's very much a two way street there.

This was particularly the case for the agenda of the SGDP, and for its work on complex gene environment interactions:

In those days [1970s], the idea that you could map genes for all these things was very much in the future, but now we really are starting to identify the biological basis of behaviour and we're still very much in the foothills. The actual useful outcomes are still a long way in the future and may remain in the future, but I think great strides have been made in the basic science. My personal view is that it would be something of a mistake to try and grasp the end game before we really know the territory. I don't think the advances we're making in genetics right now have immediate application. I really don't think that. Although we're starting to identify these genes that underlie disease, I don't think they explain a whole lot of risk in the population. It's not the case that the gene variants we know about, even though they're associated with disease, they only explain a very tiny proportion of risk. I think they're more useful in how they tell us about the biological underpinnings, as it is. They set a new research agenda, but we're still right at the beginning of that process. The pyramid up from basic science up to translational science and finally to clinical end points, we're one step up but we're still very much in the basic science bit of it, and I think to have a top down initiative to try and grasp the gains now is premature in this field. In other fields, maybe that's not the case but I think you need to build up that research base until you're close enough to the top that you can make that leap into clinical science. I think translational science is a bridge between that basic science and the clinical science. But, in psychiatry right now, it's a bridge too far.

Indeed, for this interviewee, while the emphasis on translation generated funds and other important resources, it could pose a threat to the necessary basic science:

I think there are conflicts of interest in this kind of thing and I think, if you suddenly introduce a lot of new money specifically to translational research, that ruffles feathers because I think that it's a relatively sudden shift on top of a background of, already, large amounts of change in the way that scientific, and specifically biomedical research, is funded. Some of these changes are very good. ... Large amounts of new money for infrastructure, lots of new scientists, exponential growth in the amount of publications that have gone out. So, there are some very positive developments, and I think it's understandable that you can provide these large

sums of money once you see something out there but at the end of the day, I think there is a concern that the health gains are increasingly hard to win.

The role of the SGDP – gene-environment interaction

The kind of work done in the SGDP raised particular problems for an emphasis on translation, in the eyes of some:

Genetics research is not something that you can really count on to have something to publish because it's a Will o' the Wisp. Some years you get a finding and some years you really don't. It's rather elusive...We reason forward as best we can from how the environmental causes are known to affect the body and the mind biologically to identify genes that might be in those pathways and look to see if there are any variations in those genes and if there are, if that's the vulnerability or resilience factor. Most of the time it's not because what's basically lacking here is we know a lot about the environmental risk factors but hardly anything about genes and you're working on pure hunch instead of solid theory.

But many stressed that this conceptual change was really one of the key contributions of an institution like the SGDP. For some, this was the prescience at the very root of the institution:

I think Michael Rutter, who founded the centre, was a visionary and I think he is one of the first people to realise that gene-environment interplay was important, and that it wasn't really how much something was heritable, but it was about how the genetic risk was mediated that was important. And I think he was very, very influential in guiding researchers into thinking about the fact that genetic effects were mediated through the environment, and I think that's a vital insight and I think it's one that has borne fruit in all sorts of unlikely areas.

And for one person who had left the SGDP and later returned, this was shown by how the whole field had changed:

The field has really moved on in the five years that I was away, and those papers [Moffitt and Caspi] came out just as I was leaving. Since then, it has sparked a very great deal of interest in research into gene-environment interplay, and I think that's, if not the primary focus of this centre I think it's up there, is on how genetic and environmental influences conspire to produce risk of disease.

And, for some, this had very real translational possibilities, but these were less specific applications than changing the way in which mental health issues were understood:

I think that's been hugely important in putting a kind of developmental dimension into people's thinking. It also suggests [something that ... a lot of work would, the burden of a lot of other kinds of chronic disease tends to be weighted at the end of the life course. Our hearts go wrong and we stop being able to do lots of things. In terms of physical health things, you're looking later in life for them. The major burden of mental health things is very early in the life course, so it gives you a view overall of where the key times to be looking at what's going wrong, and where you might intervene.

Once more, then, the translational emphasis that is expressed here relates to complex policy changes, and perhaps educational changes, that might impact on the early experience of children in their homes, rather than the development of medical products or specific psychiatric therapies. But once more, the translational pathways implied are hard to map, slow, dependent upon political contingencies and on many factors far beyond the competence or sphere of action of all but a very few biomedical researchers – although of course there are notable exceptions of researchers who have gone on to take senior and public positions in policy debates (as indeed has Sir Michael Rutter and, in another context, Professor Lord Richard Layard, to whom we referred earlier). However the problems of developing evidence based policy are well known and the history of translation of research findings into social policies is not particularly encouraging, given the multiple other political and economic pressures that shape the process of policy development.

It is just presentational

Undoubtedly a number of our interviewees were rather cynical about the current rhetoric of translation and the way it has been taken up by the MRC, seeing it as 'just presentational:

In a way it's internally contradictory because the MRC is really a basic science agency and they've now strengthened the more applied side of medical research, and that's the intention of the NIHR. And yet what you get from the MRC is translation, translation; you have to justify just about everything as having at least a translational aspect, and so we've tried to redefine translation to make some sense with respect to the basic research we're doing. But, basically, in a way, it's an attack on basic research; that's one way you can interpret it as a basic research unit. In the long run, the main advances, actually, come from basic research, but you have to justify basic research as being applied in order to get it funded. That's how it feels as a basic scientist, really. ... if you are doing a piece of basic research you say, how can I present this as translational?

Another interviewee also drew out the rhetorical and tactical uses of the term – it is, he said 'a shape shifter':

if you were talking to a drug company it's about, you've got these very expensive drug pipelines, they're not coming up with the new drug targets, where's your next blockbuster coming from? You've got the front end and you've got the back end. Bring that basic science through, you've got both. That would be the argument you're using if you're trying to create a collaboration with an industry partner. Now, if you're trying to get money from NIHR you're going to describe what you do slightly differently. Presumably they're more interested in public health goals at the end of the day, rather than selling their drug, so it does depend who you're talking to, what the goals are, and what your goals are affects how you describe the process. I think it's a shape shifting kind of beast, and I think people try and define translational medicine as best suits their own goals.

It's important, but not my job

Should it be the role of the researcher to take the initiative in translating their work and drawing out the implications. For one of our researchers, however important this is, it was not her role or perhaps not her responsibility:

We put the findings out there when we get them and if someone wants to take them forward and develop them, that's great... I'm not sure what the intervention programme might be because that's not my area of expertise, to design interventions but I know that there are plenty of people who have translation research grants who design these interventions but this provides in a way the

empirical evidence that the interventions should not just be focussed on the underclass.... we tend to put those findings out there and then in hope that someone with more direct translational expertise will pick up on them and use them.... Funding agencies are a little bit better about that, starting to have workshops and conferences to get people together to talk about what is the state of the science and how it could inform intervention so I think they're doing a little bit more of that but it's not something that I really have the connections to learn how to do. I wouldn't know how to approach a... I wouldn't even know who to approach if I had a finding that I thought could inform treatment. Apart from publishing it, I'm not quite sure what I would do.

Indeed, this issue of expertise in translation was referred to on several occasions:

I wouldn't have any expertise in taking it forward...I usually don't know who the audience might be. That's, I think a difficult thing for a person like me, not having the, how shall I say this, I think universities have gotten very, very au fait in the last ten years about working the media. They have now all hired press officers. They now have media offices. They have agencies such as the Royal Institution.¹⁴ They offer courses for scientists on how to be interviewed by a journalist but that is more courting attention rather than trying to get research findings out there to policy makers. In a roundabout way if the policy maker happens to read the newspaper and see that some science has been covered on the science pages, it will get there but I don't find that I get a lot of help from my university at how to say if I write a paper for a scientific journal and it's full of formulas and math and it's very esoteric and only another scientist could interpret it, I don't have someone coming from King's who has been helping me write a version for the policy maker that can be read by a different sort of audience.

Another interviewee, in response to a preliminary report containing this quotation, pointed out that the final point was unfair, since the College did have a very active and effective press office. But, never the less, the central idea represented here does stand: that there are limits to the extent to which a scientist may put findings 'out there', limits which are to some extent practical, to some extent related to how one views one's profession, and to some extent related to competencies (the idea that converting findings into policy is outside of the scientist's typical range of skills).

Another interviewee, keen to have an influence on policy, stressed the importance of working with a 'broker':

I tend to think for the things that I've been interested in that it's useful to have some kind of broker. A person who's better at the interface, who knows about the policy, who knows how those people think. And also understands a bit how I think and can stop me nitpicking on. And pitch at a level that they would be interested in.

You can't build it in – indeterminacy

If there was one general theme stressed by many of our interviewees, it was the ineradicable indeterminacy of scientific research and its pathways to applications in practice. It is worth giving a number of examples of this:

The first theme stressed by many was the time frame of the process and the multiple inputs to it, often not understood by those who advocate a criterion of translation:

When I was [in a senior position with a large medical trust] the lay members ... were ... arguing very much that we needed to find out what good all of this was, what benefit there was. And at one level, that's an entirely reasonable question, but where the unreasonableness came in, is the assumption that you could do that on a project by project basis. Not only do you not, but you should not change a policy on the basis of one study. Even the best study needs to be within the context of other research. And so looking at the basic science that you funded to Doctor X five years ago, has that led to patient benefit, is a daft thing to ask. How would you know? If it has led to benefits, it will undoubtedly be because it has fitted in with other research, other basic science research, but also other cognate research. So that's one issue. The other is how long it takes, so that if one looks at smoking and lung cancer, it took 60 years for a general acceptance that this wasn't an odd fact. It was fairly clear much earlier on that it wasn't, but it took a while to convince people. So that in looking at benefits, you've got a long timeframe and you have multiple sources of evidence, some of which, the thinking mainly derives from basic science; some of it, it doesn't.

The same point was made by another interviewee:

Well, I mean, we are trying to understand a very important disorder that has a major impact on society and on the individuals concerned and as long as the

research has done very well, scientifically, using this very hypothesis-driven approach, then, yeah, then there's the hope that it will be useful in a more direct translational way, as well, in the future. Yes, often it is difficult to see at the time of doing that, how exactly it will be used, because it's only going to be one part of the picture that's emerging.

And another used this as the rationale for his focus on 'understanding' as the key issue:

the fundamental thing about basic research, so what you really want to judge, as a scientist, I think, is it going to advance understanding. And, obviously, we're working in fields that are related to things that people want to know about for practical reasons, like behaviour, what's the biochemical machinery, what are the genes behind it and that there are applications like drug targets for which there is a crying need. But it's still all longer term and indirect eventual benefits and you don't know in detail.... I guess the hardest thing to estimate is the time scale, and if you really focus on things that can generate the translational thing in a short time scale, you're focusing on the small incremental advances, if taken to the extreme you'd just be optimising existing medicine which possibly doesn't have the same prospects of major advance. ... it's quite hard to say in very specific terms, well, we discovered this gene function in mouse and that's allowed us to find a therapy or something in human that such simple stories. Probably, if I had more imagination, I could come up with one, if I read the literature more thoroughly. But it's more a matter of the building, body of knowledge. Don't get me wrong, you're motivated to go into science to find things out that might well be of use to humanity; [but] it's on what time scale and in what detail...

Thus policy makers, like clinicians, had to make their decisions on funding research in situations of very imperfect knowledge:

As a clinician, the next patient I see, I have to decide what I do. I can't say, well actually, we need a bit more research before I can decide how to treat you. I've got to take a decision. And that decision is based on the best assessment one can of the evidence, but it involves a certain action on uncertain knowledge. And that's what policy makers have to do. They similarly have to say, we can't wait another five years for research. Whether we like it or not, we have to decide whether we do this or whether we do that. And as in clinical medicine, a decision not to act is as much a decision as a decision to act. And that's true for the clinician and it's true for the policy maker.

Even when things appear to have a policy relevance, the relations are complicated and difficult to predict:

I've worked on things that, I think, have pretty immediate policy implications; then I've worked on other things that, I think, the actual translational implications are pretty far down the road. For example, I worked on a project several years ago now, where it was very much motivated by welfare reform policy in the US, and the part of welfare reform policy that was driving a lot of money towards promoting marriage for low income couples. The motivation for the policy is that kids who were raised in two parent families do much better than kids who were raised by single parents. The point that I was trying to draw attention to was, it really depends on who your parents are; so it was analysis that showed that when you take fathers anti-social behaviour into account, it's true that if you have a father who engages in very low levels of anti-social behaviour, the more time he's been living with the family the better off the kids are doing. When you have fathers who engage in very high levels of anti-social behaviour, actually, the more time he spends living with his kids, the worse off their kids do. but the gene environment interaction stuff, for example, I'm not sure what the translational implications of it are. I don't know how useful it is for clinicians, right now, in the sense that certainly it does identify sub-sets of people who are particularly susceptible to environmental risk factors; but I'm not sure what clinicians are meant to do with that information exactly. I wouldn't recommend that they run out and genotype their patients, because it's not a strong enough predictor of outcome that I'm sure would be worth it for them to do that. That raises sort of ethical problems anyway, if what you're talking about is interaction between some genetic variant and maltreatment, for example, you want to prevent people from being maltreated, whether they're particularly genetically susceptible to it or not.

Another of our interviewees also stressed this ambiguity:

I don't think people here realise that they're already doing translational research.... I wouldn't really characterise the bulk of what I publish as being translational, in either spirit or intention. But, on the other hand, it's been cited ... in various contexts that can be called translational, in relation to clinical guidelines for treatment for specific disorders and stuff like that. So, I think genetic research does have application in various ways in informing clinical goals, even if it doesn't directly lead to improved clinical care, it informs what doctors do and what we know about disease, and I think that's useful and I think, in some sense, it's translational.

The same interviewee stressed that the 'translatability' of basic research findings often occurred in a timescale, and with implications, that were not, and perhaps could not have been, foreseen by the researchers themselves:

[In some of our research] we were able to show that those who subsequently became very seriously involved in a career of violent crime had been lagging behind in their neurological development as adolescents, quite far behind, and this is in some papers that we published in the 1980s and 1990s. [We] were interested in a basic science way of trying to understand are there factors within the individual that increased the statistical probability of violent reaction to a social situation. ... some law scholars at the University of Virginia wrote an *Amicus Curae* brief for the United States Supreme Court using our research evidence to make the argument that juvenile violent offenders don't have the brain maturity to be tried as adults. Now there has been a movement in the United States of more and more punitive juvenile law and in fact the death penalty, capital punishment was applied to juveniles in many states and so some kids under the age of 18 have been executed. So this was used to successfully argue and overthrow that in the Supreme Court, so now it's not legal anywhere in the United States to execute a juvenile offender - on the principle that their brain could not have been mature enough for them to be responsible in the way that an adult offender is. I think that's a fantastic social policy application that I could never have foreseen when I was doing the research. I did the research for my own reasons and my own curiosities but these legal scholars somehow saw something in it that I would never have seen.

It's changed the way I think

It is clear, however, that for some, the emphasis on translation has changed the way they think about research. A long quote from one of our interviewees illustrates this move from scepticism to commitment:

I was very sceptical of the whole translational research phrase when it first came out. I was interested in the history of it because it first leaked into the public consciousness in the United States. In part that was because there are certain very influential senators in government who are constant critics of the National Institute of Mental Health and they ... have what's called the Golden Fleece award, where each year [they go] through all the research grants given by the National Institute of Mental Health to find ones that had funny titles and then made public spectacles of the scientist and gave them this Golden Fleece award that they had ripped off the taxpayer by endlessly spending tax money on blue sky basic research that would never lead to helping people or improving treatment. So these figures in government I think are well meaning in holding funding agencies' feet to the fire saying what are you doing for the taxpayer with their money? Mental health research is an easy mark. ... People feel that a lot of progress has been made in treating cancer. A lot of progress has been made in preventing heart disease but what can we do for their child

with autism? There's a kind of public perception that mental health is still a great mystery. And it is..... the National Institute of Mental Health developed this whole notion I guess maybe 15 years ago now about translational research and the idea of translating from bench to bedside and making a big hoo-ha out of it and everyone was encouraged to add a translational aspect to their draft proposals and there would be special funding for translational research. ... And what I noticed is that many of my colleagues who were doing the same old, same old research they always did but now calling it translational research, so there was the extent to which there was any real movement into more treatment orientation by researchers I think was a bit patchy in those early years. ... there was some kind of cynicism. That said, I think it's been a very healthy movement and I'm happy to see it come to the UK. I think that mental health research has a bad reputation with the public and if the public can be convinced that we are making a serious effort to really create treatments that work, that's great.

Because of the translation movement, I think more and more of the possibilities earlier and earlier in the stage of a research project, I think about is there something I can do in the design of this study that will increase the chance that it will lend itself to translation so it does... I don't want to stop the longitudinal research or the genetic research that I do in order to become a person who designs social policy or writes legal briefs or runs randomised clinical trials. I don't think that's my area of expertise and there are people who do that quite well so I'm happy for them to carry that kind of stage forward but because of the translation movement, it means that I now think earlier and earlier in the research process about the possibility that there might be somebody out there who would be wanting to use this. And I think at the beginning of my career I didn't think in that way.

Translation in practice

Even where translation had occurred, in the eyes of the researchers, for most it was not a simple pathway from bench to bedside:

I think it goes both ways, there are these scientific issues that we are investigating which have an impact on how adult ADHD is viewed, but also sometimes clinicians come with thought from their clinics, particularly looking at issues such as [unclear] morbidity and thinking, what are the reasons why we see such high [unclear] morbidity in these ADHD cases that end up in adult clinics. And then they have started projects studying that in more detail, because it has implications for treatment....

Some researchers did give examples of very direct input into policy, but commented that this did not gain much academic kudos:

I've occasionally been invited to go to meetings in X local authority and talk to the chief officers and people like that. Just for me to say there's a lot of it about really, that kind of level. Just because of the kinds of phenomena and the stage we're at in understanding them, which is pretty basic; and where the world is at in thinking about them, which is also pretty basic. It's at that level of relatively simple conversations.... [but] you don't get a lot of academic brownie points for going and talking to the Chief Officer of X Council. So I don't do it a lot. From my point of view, having a system where you did get brownie points for that would make more sense actually. [tension between academic brownie points and translational ones] Particularly if what the translational activity might be, not for but it could be for some people: write a manual for teachers. That is not going to look good on the RAE. But it might be terribly important actually in benefit to humankind.

This interviewee raises a point that we have heard on many occasions in different contexts – that the structure of reward and recognition in the research community has a significant effect on the priorities given by individuals to different potential activities, and that some translational activities – in this case input into the details of local policies, is not highly regarded.

Another area of potential translation in biomedicine, which has been much discussed in relation to the contribution of neuroscience researcher to psychiatric practice, is input into diagnosis. One very senior member of the SGDP was sceptical about this:

there have been those who see genetic research as having its big impact on classification and diagnosis, and hence there are people concerned with the [revision of the DSM - the American Psychiatric Association's Diagnostic and Statistical Manual, the next version of which is due out in 2012]. I don't see that as translation.... It's a way of the American Psychiatric Association bringing in large funds

This interviewee felt that there was a very large distance between basic science and the role of diagnosis in professional bodies like the American Psychiatric Association, or

those involved with the International Classification of Disease (ICD) But others felt that this was an important aspect of their work:

The other things that I've done that have been translated, because they're older is simple sorts of tests of social understanding that can tap in a diagnostic situation what you would otherwise have to go and sort of follow a person round in the world to see that they're messing up in. ... [e.g. of implications] the teacher was so astonished that, in the course of the diagnostic assessment her attitude to him really changed completely, she could see that he was a child who had a core disability and was as deserving of sympathy and time and effort as the child in the wheelchair or the child with dyslexia or whatever rather than he was an obnoxious know it all. ... I'm on the work group of about 12 people for the new DSM-V - DSM - V is coming out in 2012, they have workgroups on all the specific disorders such as ADHD and so on, and I'm on the one for pervasive developmental disorder and autism and other related things. So, we are deciding what the diagnostic criteria will be, and, yeah, so this information is feeding in; we don't know yet what we'll conclude, but it is affecting diagnosis.

This implies another translational pathway, and one that is rather difficult to quantify – that of giving advice to relevant bodies that set policy in specific areas. DSM is not the only diagnostic publication that arises in this way from discussions among professionals about relevant criteria – in the UK, one key body is the National Institute of Health and Clinical Excellence (NICE):

Well, ... some of my papers have been quoted, for example, in NICE guidelines, so the National Institute for Health and Clinical Excellence, guidelines for ADHD, I think it's in press now, so some of my own research has been quoted there. So influencing [?] the guidelines. Another of my papers has been quoted in the European guidelines for hyperkinetic disorder, 6th edition, or whatever it was, and there may be more examples. I'm not even aware of these, and I know that the administrative staff here are, are doing searches on issues like [unclear] always aware of this, so I know that some of my research and many, much research from my colleagues here, has influenced the diagnostic criteria.

Indeed, the potential implications of some of the SGDP's research were considered by some to be very radical, undermining the idea of discrete psychiatric diseases in favour of multiple dimensions:

a lot of people here arguing that there aren't real psychiatric disorders, at least in many of the cases there aren't, and the argument is applied to ADHD, for example; that's it's just the extreme of a continuous dimension. So that's one of the, I think, big things coming out of the centre, is that we've shown that to be, that there's a lot of evidence that supports that view.

And, for some researchers, this made the communication of the results – translation into the public domain, particularly difficult:

[when talking to the media about our research] ... the first thing they often say is, does this mean that autism doesn't exist? It is a challenge to the typical way of doing molecular genetic research in autism, and huge amounts of money go into looking for the genes for autism, of course. The suggestion from our research would be that if you go looking for the genes that contribute to autism, as a package, you're a bit onto a loser already and you're much better off looking for the genes that contribute to social impairment and social skill specifically, or the genes that contribute to communication disabilities.

Translation in a system of worth

As we hinted in the previous chapter, it is possible to understand the translational imperative within what one might term 'a system of worth' for doing scientific research – that is to say the critical and justificatory operations that people perform in their everyday lives and work, and the principles and criteria that they appeal to in order to rank, prioritise and justify their actions and their choices.. The problem of translation is not simply one of the configuration of basic research into outcomes that can be seen as 'improving the health and wealth of the nation' – to quote the slogan of the National Institute of Health Research. Rather, it is one of marshalling different systems of worth, and of aligning different and possibly competing systems of value. We came across a broad range of principles underpinning different systems of worth for doing research in psychiatry in particular, and perhaps for doing scientific work in

general. Many would probably agree with the statement by a very senior member of the SGDP:

one of my motivations, over half a century being involved in research, is that it has some benefits. So I have no problem whatsoever with the notion that we should be concerned with that. I do have concerns about the simplistic way it has sometimes been interpreted.

However this general motivation is capable of multiple interpretations. At one end of the spectrum, a researcher commented:

My motivation is that I want to understand, and I'm not here because I want to improve the lives of a particular group of patients, although I think that's a great aim. I'm a basic scientist...and I think for me, in the past it's always been more of the beneficial spin-off: helping patients would be something that someone else would do.

At the other end of the spectrum, one of our interviewees argued:

if you can ask yourself a question, how is the research that I do ever going to benefit anyone, other than just provide more interesting ideas? If the answer to that is it's not going to benefit anyone, then you should probably be doing something different. From my own satisfaction I would find it pretty upsetting to come up with the answer where it doesn't do anything other than generate interesting ideas.... I do believe that knowledge has value in itself absolutely, but for scientists working in our kinds of areas, with disorders, if you said, well, I want to find out X, but it's not because X will lead to Y, and eventually, however far down the path, it will help someone, it's pretty strange that I just want to find out X and actually it's never going to be of use to anyone, I just want to know. I think, it's perfectly valid to do that, but I don't think the Medical Research Council should pay for it. ... If I, at the end of my career, felt that what I had done had never made anything better, for any of the families who have children with autism, or individuals with autism, even if it was only at the level of, this is better understood, so they're less ignorant, and the teachers bully the kids less; if I felt that nothing had been achieved, I would be terribly upset, I would have wasted my time, even if I'd found out lots of interesting facts

Of course, any individual's personal system of worth is shaped by many factors, some personal and biographical, some intellectual and ethical, and some personal and

biographical. Thus this same researcher went on to describe how having children was the main factor in becoming more interested in translation:

Becoming a parent, you become a lot more reflective...When I went on maternity leave, both times absolutely determined I'll come back full-time and to do whatever work I could do in the maternity leave, it is still a time to reflect on the work you do, and is that really more important than looking after your own children. And so when you're removed from this actual environment of being so busy day to day, you have a bit more time to reflect on the meaning of your work, and so on. And so, I think, that for me was probably the biggest individual change, in terms of really reflecting on the meaning of what I do, and how it's important, and also becoming aware of these issues relating to children and schools and so on through having your own children.

This would seem to indicate a simple way of enhancing translation: more of the point of view expressed by this interviewee, with its emphasis on usefulness, and less of that expressed by the former with its emphasis on understanding;. However this would be too simplistic. For one thing, the former view is invariably associated with a 'side-effect' model: the discoveries of basic scientists will be taken up by others in clinical applications. But, and perhaps rather more importantly, the real value of the institutional setup of the SGDP is a system of interdisciplinarity or *transdisciplinarity* that permutes not only the social, genetic and developmental, but also these different and apparently conflictual value systems.

Translation and interdisciplinarity

In our discussion of the stakeholder interviews, we suggested a way to go beyond the metaphor of barriers, via an new approach to agency, actors and objects. This has much to offer for our understanding of our case study. For example, the character of the SGDP is a compound of various elements: its history, its architecture, its fixtures and fittings, and its commitment to fostering felicitous forms of interdisciplinarity under the stewardship of its directors and senior members.

The importance of all of these comes across time and again in the interview data in fragments such as these:

No, I think there are so many things that I just couldn't do on my own and I think collaboration is absolutely essential.

There is a lot of collaboration, yes. You can't do this kind of stuff on your own really. Well, it would be very hard; partly just in terms of getting ideas but partly the sort of stuff I do requires longitudinal data.

That was the whole notion, and that you do that much better if the person's along the corridor. You can have your collaborators in Kathmandu if you want, but you actually get much more bang for your buck if you can talk to people over coffee. Yes, that's exactly the whole idea.

Here it has been fantastic actually, because everyone is around on the same corridor. I think the building design has helped a lot, because in the old days, we were in the other building and it was long, dark corridors and people kept their door shut. We were supposed to keep our door open, but a lot of people do have them shut, but at least, you've got glass, and people can look through, and you can wave at them and everything like that.

The building's significance is related to and explained in terms of its history:

Initially the centre was scattered in odd rooms across six buildings and they were all sort of within range, so it was perfectly easy to arrange appointments to see people. But what you didn't have is the informal conversations which make you realise that the person working two doors up is actually doing work that you had no idea was relevant to what you were working on. So when X and I first discussed the possibility of the building, before funds became available, we were both very firmly of the view that it needed to have a structure that encouraged informal interactions. And I think it does. Its a nice building. Its easily the nicest building I've ever worked in.

Working in a purpose-built environment rather than a building that has legacies of other former uses implies a certain sort of a history for the Centre, that is followed through in its origins, its naming, and its initial recruitment strategies:

[The Centre] was created because the MRC had closed down two MRC units in social psychiatry for good reasons, but was concerned that there was a need for, as it were, for a modern social psychiatry...the roots were, if you like, in the concern over

social psychiatry rather than out of genetics. Now, it did seem to me that an understanding had to involve genetics, and hence that's part of the title of the centre. It also had to involve development... At the time it was funded, there was scepticism as to whether we could recruit people at top international level. And the review committee was sceptical and said you'd be fortunate to do it at senior lecturer level. They would say they're not interested in that. It required international leaders; its international leaders that we will recruit. And so people like Robert Plomin, Judy Dunn, Avshalom Caspi, Terrie Moffitt, they were at the time, and still are, the worlds best in this. So it was quite nice to see. Once people can see the intellectual excitement and that its doable, then. And of course, every recruitment that worked helped the next recruitment.

And, for many, interdisciplinarity is itself a form of translation – here translation across different levels and types of research – for instance from epidemiology to genomics, from experiments to clinical observations, or from animals to humans:

I think, the value of the centre is in trying to do this research across different levels of analysis, and that much of psychiatry and psychology has been characterised for a long time now by this division between the biological sciences and the social sciences. The reality is that it's far more complicated than that and these risk factors interact and these protector factors interact across lots of different levels; so I love the fact that people here are actually trying to identify those kinds of more complex interactions. I think, there is some value in actually demonstrating that that is what's going on, and, I think, eventually it will translate into one of the drug treatments of psycho-social treatments or whatever they will be; we're not quite there yet.

Indeed, interdisciplinarity and translation into clinical applications, are, for some, very closely related:

I think, in order to get the advances that you need out of basic science, you do need to put these different research areas together, because you're not going to get the advances solely from looking at either, looking at the genes on their own is going to tell you something about yeast or flies or mice, but that's not going to tell you about human health. I think, the biological processes themselves, because they have their effect within the context of our lives, specifically in terms of psychiatry our social lives, I think these are absolutely inextricable and I think any attempt to gain advances from that has to take the whole...

There is also a sense that this is where new generations of researchers would derive a feeling for interdisciplinarity. One interview expressed this view:

I think, that's where you will really get the interdisciplinarity by training the young minds to know about all of it. Otherwise, it's really just about us being non-ignorant enough to be able to communicate with each other, but not, of course, be experts in it. But students grow up actually understanding it all, which is fantastic, so that's been a great pleasure to me to, to be mentoring young people who can teach me those different things.

The placing together of the 'young minds' of the juniors with the double negative 'non-ignorant' is particularly interesting, for it indicates that what is natural for the young mind is, for the senior researcher, the compensating for an absence; this connects neatly the two kinds of translational activism discernible at the SGDP: the one dispositional, based on a personal commitment, the other in a sense counter to one's disposition, but nonetheless to be valued from institutional loyalty or pragmatism.

The interdisciplinarity of the SGDP, and its institutional structure and architecture, had enabled it to forge a strong identity, to which most of our interviewees were committed. Such strong identities can work in two different directions, of course, since they may either give the organization confidence to approach new ideas and challenges such as translation on their own terms or they may create a sort of enclave with more of a resistive siege mentality. Initially, with respect to translation, one might have expected something of the second of these, but what emerged, rather, was a sense of the malleability of the idea of translation at the Centre. One interviewee said "we define the field, so we define how it is to be translated."

Conclusion

Overall, then, we found a variety of views among the practising researchers at the SGDP about how they saw 'translation'. For heuristic reasons, we can group these into five general themes:

1. Rhetoric: Translation here is seen either as a piece of jargon currently in fashion, or as a way of re-describing research as a means of securing funding.
2. What we have always done: Translation here is seen is a term applied to what basic scientists have always done, which is to aim to produce results that have practical implications.
3. Fundamental: All research should be translational in its aims; research should not be done for research's sake or for its curiosity-value.
4. Orthogonal: Translational goals are different from those of basic research; they may, however, be linked together in such a way that advancement of scientific knowledge also produces benefits, albeit as a side-effect.
5. Translation versus application: Translation, in its widely accepted form, confuses two distinct processes: applications (treatments, for example) and the propagation of findings from one field to another.

We can see here that even in one rather narrow branch of potentially translational biomedical research, that is to say the psychiatric research carried out in one centre of one specialised psychiatric research institute, there is little agreement about what constitutes translation, let alone on how it should best be achieved. What we see, instead, is that individual views can best be understood by locating the translational disposition of actors within their own individual systems of worth, the way in which they chose, justify and legitimate their own activities and research priorities, and the way in which they give meaning to these activities in their narratives, which are fundamental to their very identity as researchers. It would appear from this analysis, then, that if the imperative of translation is itself to translate into the activities of those

actually undertaking the research, the success of this process will depend on the ability of all those involved to both recognise, and to align, the diverse economies of work that characterise the research environment.

5. BIBLIOMETRIC FINDINGS ON TRANSLATION AT THE SGDP

This chapter examines the question of translation by means of an analysis of the research outputs of researchers at the SGDP in peer-reviewed articles using bibliometric methods. The main focus of the analysis is directed towards the 'gaps' in translation identified in the Cooksey Review (Cooksey 2006: 86):

The first gap arises in the translation of basic and clinical research into ideas and products; and the second relates to introducing those ideas and products into clinical practice.

In this chapter, therefore, we adopt a rather specific conception of translation, which refers to the interchanges and transactions between basic research and clinical research. The principal tool used to assess the extent to which such gaps exist at the SGDP was the classification of publications according to the extent to which they focus on clinical research or on basic research. In order to assess this, we use a measure called 'research level', which we describe below.

Bibliometric data

The core bibliographic data used come from the ISI Science Citation Index (SCI) and Social Science Citation Index (SSCI) databases. Records were gathered using names as search terms for each researcher based within the SGDP, past and present. Some bibliometric analysis had been conducted by an SGDP member in 2004 (Schalkwyk 2004); this was used as a reference to check that an accurate volume of records had been retrieved and it also provided a useful comparison for the analysis.

The search terms were designed to optimize recall (the proportion of relevant documents retrieved by a query) in the first instance by searching for a list of family

names of SGDP researchers, limiting the search to records with London in the institutional address and to dates later than 1992. This resulted in approximately 6500 records, which were cleaned up using a series of programmatic methods to filter out false positives. These filters were designed to be conservative, and to avoid false negatives, and each record removed was hand-checked to ensure that it was correct to remove it. Finally, the remaining records were checked by hand for inclusion or removal from the list. Subsequent correspondence with SGDP members identified a set of missing records for one individual with a common name and a broad range of research interests; these were added to the data set, resulting in a final set of 2134 records for analysis.¹⁵

These data were augmented by other bibliographic records (in the order of 500,000) collected for particular aspects of the analysis. Some of these were required to calculate research levels, others were gathered to examine the research levels of publications referred to in SGDP articles, of articles citing SGDP articles, and of articles by collaborators with the SGDP. Details are given at appropriate places in this chapter.

Classification of publications from clinical to basic: the research level indicator

In order to explore the ‘gap’ in translation identified in Cooksey, we applied a measure that helped us understand the distribution of SGDP research along an axis from ‘basic research’ to ‘clinical research’. The technique that we adopted was to apply a measure known as ‘research level’ to the publications arising from SGDP research, to assess the extent to which this was published in journals specialising in basic or applied research, or was taken up in basic or applied research undertaken by others. Other citation analyses using this indicator also helped us explore the patterns of collaboration between researchers across the spectrum from basic to clinical research, and indeed the

extent to which any one researcher incorporated a kind of translational ethos, moving across this spectrum in their own work

The research level concept was introduced initially by Narin et al. of Computer Horizons, Inc. (CHI) in their 1976 paper *Structure of the Biomedical Literature* (Narin et al. 1976), and it has gained considerable currency since then (Grant et al. 2000). While attempting to classify biomedical fields, it became apparent to them that features of citation patterns amongst fields suggested the introduction of a spectrum of research orientations from basic to clinical. They defined four levels to characterize these different orientations (Narin et al. 1976: 29):

1. Clinical observation

A journal concerned principally with observation, rather than research
(exemplars *Journal of the American Medical Association*, *British Medical Journal*)

2. Clinical investigation

Clinical, but with a strong research orientation (exemplar *Journal of Clinical Investigation*)

3. Clinical mix

An even mixture of observation and investigation (exemplar *New England Journal of Medicine*)

4. Basic

A journal concerned with fundamental research, which “cites overwhelmingly other journals within its own area of fundamental research” (exemplar *Journal of Biological Chemistry*)

The CHI classification has two drawbacks. First, it is a categorical variable, which means that there are no intermediate values between levels, so one cannot make finer-grained distinctions between journals. Second, it relies on the use of a panel of experts to classify journals, which, amongst other problems, means that the research level of a journal can easily become out of date if the nature of the journal changes after classification.¹⁶

In their paper *The Classification of Biomedical Journals by Research Level*, Lewison and Paraje (2004) suggest a method of calculating research levels for a journal directly from titles of articles in that journal, the assumption being that an article's title will contain a high signal-to-noise ratio of information about the content of the article (compared to, for example, abstracts or the full text of an article). This method assigns to each journal a value in the range from 1 to 4, where 1 is the most clinical and 4 is the most basic. The paper describes how this range was chosen for comparison with the CHI classification described above, but the method it proposes has the advantage that it is a continuous variable rather than a categorical one. The paper also calculates intervals within the range for the four CHI categories; these categories have been used in the following analysis where it helps clarify matters.

Orientation of journals for the publication of SGDP research

Calculating the research levels for all journals with SGDP publications involved gathering a sample of records for each journal. In total, researchers at the SGDP have published in 327 different journals, and from which 118,000 publication records were gathered. There was average of 470 records for each journal. The data were gathered initially for 2006, and extended backward and forward by years to ensure a complete coverage and with enough records for each journal to calculate the research level score

accurately. Each of these journals was given a research level score using Lewison and Paraje's method described above.

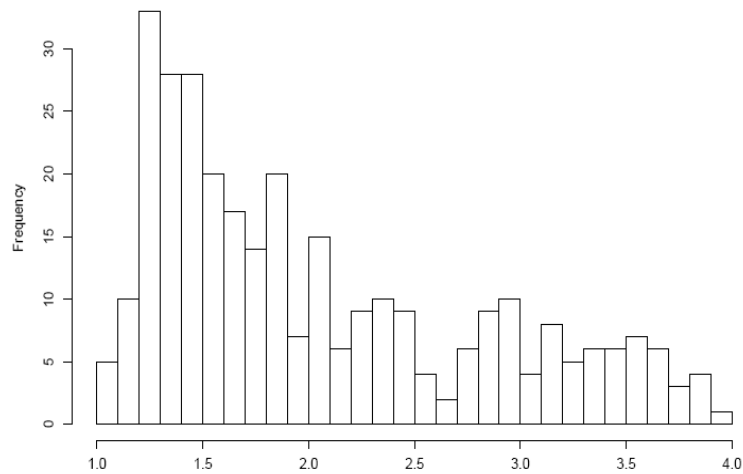


Figure 1: Research level histogram for journals with papers published by SGDP members (327 journals)

Figure 1 shows that the majority of journals that carry publications from researchers at the SGDP are towards the 'clinical' end of the basic - clinical spectrum. The cumulative distribution plot in Figure 2 indicates that, while the emphasis may be on clinical publications, the most immediately clinical (those classified as research level 1 to 1.2) are not used as much for publications of SGDP research as those which are slightly more toward the clinical investigation category (those with research levels scores in the range 1.3 to 1.5).

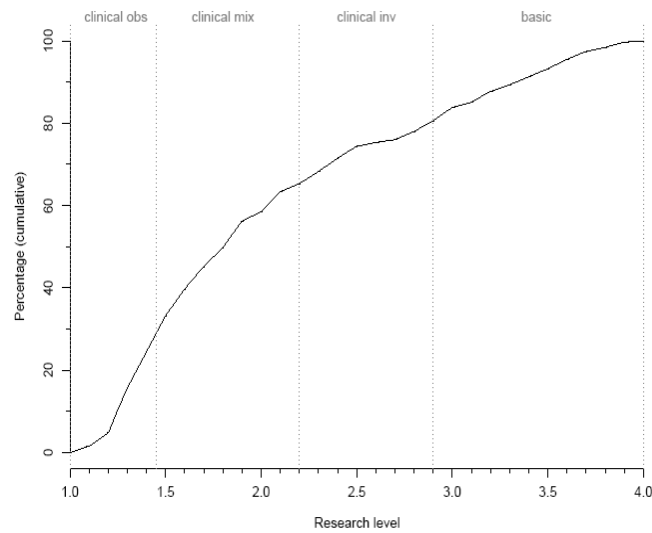


Figure 2: Cumulative distribution of research levels of journals with papers published by SGDP members (327 journals)

The main journals at this clinical end of the spectrum are tabulated in Table 1:

Level	N	
1.08	4	Child Abuse & Neglect
1.15	5	Archives Of Disease In Childhood
1.17	2	International Journal Of Language & Communication Disorders
1.17	2	Social Service Review
1.17	7	Current Opinion In Psychiatry
1.20	3	Archives Of Pediatrics & Adolescent Medicine
1.22	6	Journal Of Intellectual Disability Research
1.22	3	Pediatrics
1.23	2	Canadian Journal Of Psychiatry-Revue Canadienne De Psychiatrie
1.23	14	Lancet
1.24	2	International Journal Of Epidemiology
1.24	21	Journal Of The American Academy Of Child And Adolescent Psychiatry
1.24	2	Journal Of Consulting And Clinical Psychology
1.25	2	International Review Of Psychiatry
1.26	5	European Eating Disorders Review
1.27	3	International Journal Of Geriatric Psychiatry
1.27	2	Infant Mental Health Journal
1.28	13	European Child & Adolescent Psychiatry
1.28	3	American Journal Of Epidemiology
1.29	2	Health Psychology
1.29	7	Acta Psychiatrica Scandinavica

Table 1: Research levels of journals and number of records of SGDP publications where research level is < 1.3 and where the number of records in the database is > 1

Similarly, Table 2 shows the research levels of journals in the peak frequency range, above 1.3 and lower than 1.5, that is to say, those closer to the 'clinical investigation' area of the spectrum.

Level	N	
1.30	2	Zeitschrift Fur Kinder Und Jugendpsychiatrie Und Psychotherapie
1.31	5	Psychologist
1.32	10	British Medical Journal
1.32	18	European Psychiatry
1.33	91	British Journal Of Psychiatry
1.33	2	Australian And New Zealand Journal Of Psychiatry
1.34	3	Journal Of Developmental And Behavioral Pediatrics
1.35	5	Addiction
1.36	9	Social Psychiatry And Psychiatric Epidemiology
1.36	3	Infant And Child Development
1.37	5	Jama-Journal Of The American Medical Association
1.38	12	International Journal Of Behavioral Development
1.38	14	Journal Of Affective Disorders
1.39	2	Journal Of Clinical Child And Adolescent Psychology
1.39	2	BMC Psychiatry
1.40	57	Journal Of Child Psychology And Psychiatry And Allied Disciplines
1.41	6	Journal Of Family Psychology
1.42	2	Journal Of Adolescence
1.43	3	Psychosomatic Medicine
1.43	2	Stroke
1.44	3	Developmental Medicine And Child Neurology
1.44	3	Journal Of Child Language
1.45	2	Depression And Anxiety
1.46	2	Developmental Neuropsychology
1.47	2	British Medical Bulletin
1.47	3	Autism
1.47	26	American Journal Of Psychiatry
1.48	4	Merrill-Palmer Quarterly Journal Of Developmental Psychology
1.48	2	Journal Of Marriage And The Family
1.48	67	Psychological Medicine
1.48	2	Child And Adolescent Psychiatric Clinics Of North America
1.48	3	Cephalalgia
1.50	8	Psychiatry Research

Table 2: Research levels of journals and number of records of SGDP publications where the research level is > 1.3 and < 1.5, and where the number of records in the database is > 1.

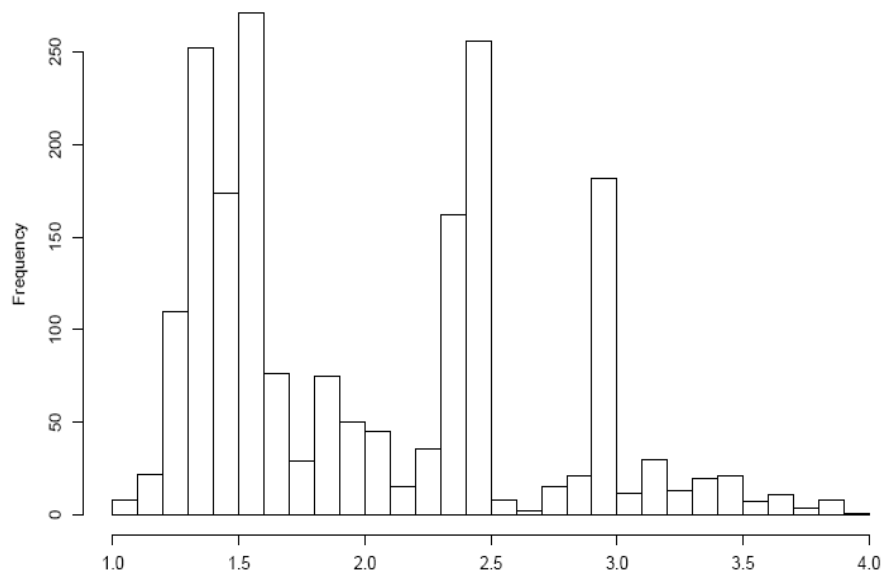


Figure 3: SGDP article research levels histogram (all years)

These data show something about the profile of the journals in which the SGDP has published. A mapping of the calculated journal research levels onto the actual set of publications results in a somewhat different pattern of distribution: the same peak at around 1.3 can be seen in Figure 3 but there are also peaks between 2.3 and 2.5 and at around 2.9. This distribution is reasonably stable over time, as can be seen in Figure 4, which shows the distribution of research levels for each year, and in Figure 5, which shows the yearly proportions for each of the CHI research levels.¹⁷

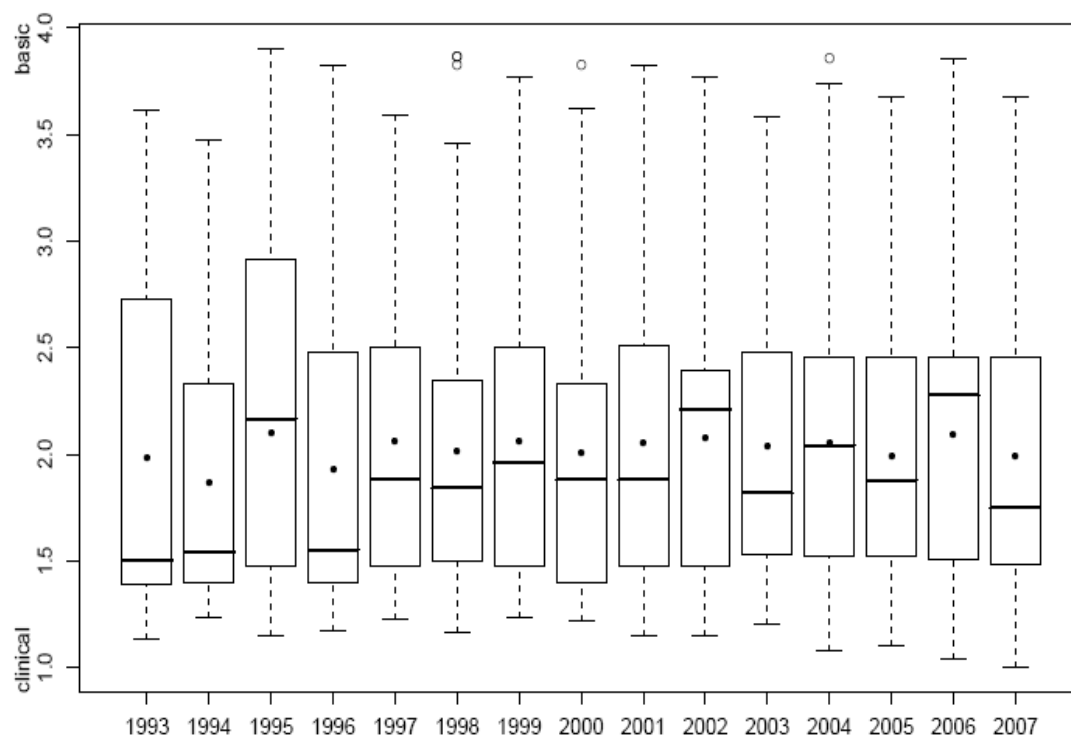


Figure 4: SGDP research levels by year.
 The • symbols show the mean for that year.
 Bars show median values

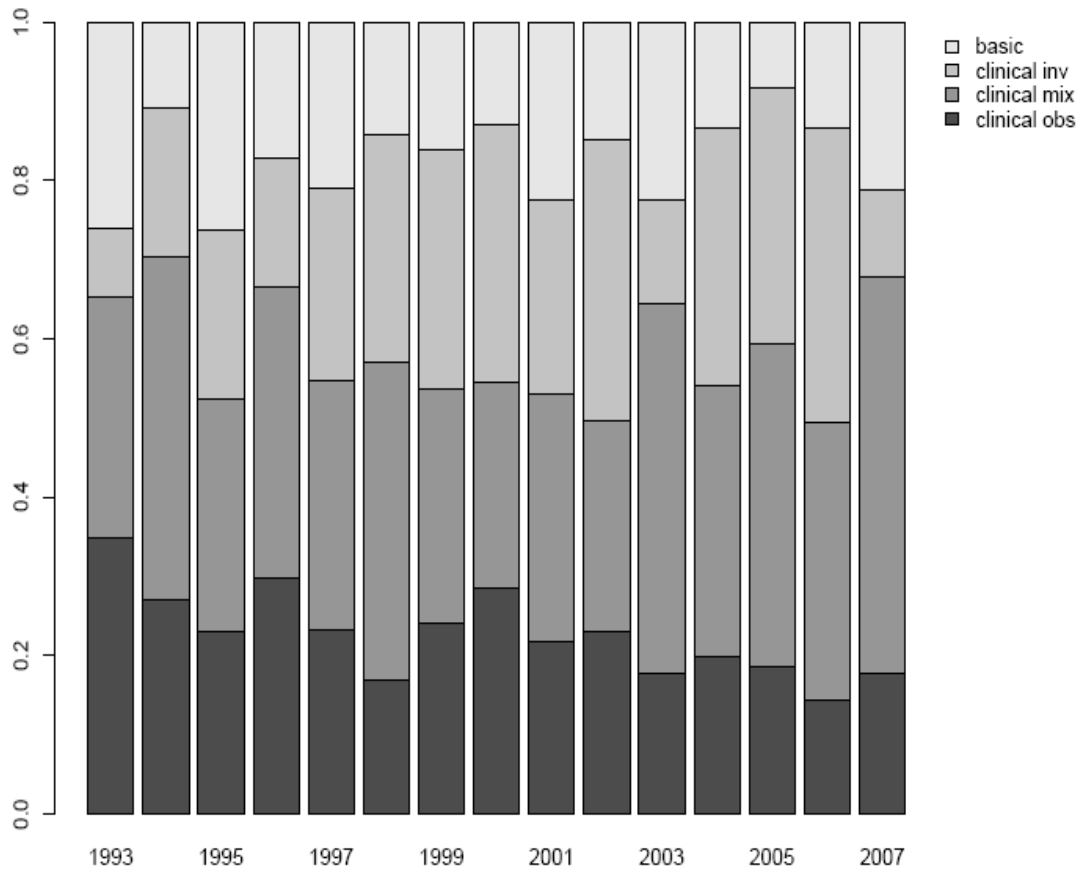


Figure 5: Research level classification of SGDP publications by year (proportions)

Publications in each of these areas are dominated by a few journals, and we inspected their web-site home pages to assess the accuracy of the classification and to gain some insight into the kinds of journals represented in those peaks. It is important to bear in mind, however, that Journals may frame their self-representation in order to maximise submissions, and the descriptions may not accurately represent their contents as measured by research levels.

The peak toward the clinical end has 81 records from the *Journal Of Child Psychology And Psychiatry*, described on its home page as “bring[ing] together empirical research, clinical studies and reviews of high quality”¹⁸, 77 from *Schizophrenia Research* (“The journal of choice for international researchers and clinicians to share their work with the global schizophrenia research community”¹⁹ and 67 from *Psychological Medicine* (“a leading international journal in the field of clinical psychiatry and the basic sciences relating to it”²⁰).

The peak in the centre has 152 records from the *American Journal Of Medical Genetics Part B-Neuropsychiatric Genetics* (“a forum for experimental and clinical investigations of the genetic mechanisms underlying neurologic and psychiatric disorders”,²¹ and 66 from *Molecular Psychiatry* (“The emphasis is on bringing together in one journal the best pre-clinical and clinical research, including research at the cellular, molecular, integrative, epidemiological, translational, clinical, imaging, psychopharmacology, and treatment outcome levels”.²²

The right-hand peak has 131 records from *Behavior Genetics* (“The leading journal concerned with the genetic analysis of complex traits...focus on both the application of various genetic perspectives to the study of behavioral characteristics and the influence of behavioral differences on the genetic structure of populations”.²³

If one takes these descriptions of the ambitions of each set of journals at face value, we can conclude that the publications of SGDP researchers are largely directed to the borders between the clinical and clinical mix categories. This choice of publication outlets for SGDP publications would appear to signal a significant interest in the translational potential of SGDP research, at least in so far as it relates the potential applicability of the findings and to communicating research results into the clinical domain.

Sources of SGDP research – citation analysis

Following the same procedure used to track the publications used for SGDP research, bibliographic data were gathered to calculate the research levels of articles cited in the SGDP articles (a further 180,000 records). Figure 7 shows the relationship between the research level of each SGDP article – that is to say, the place of the journal on the spectrum from basic to clinical - and the mean research level of references from it – the location of the references utilised on the spectrum from clinical to applied. This gives some indication of the translational work done within the publications themselves, and the extent to which they engage in transactions between basic and clinical research outputs.

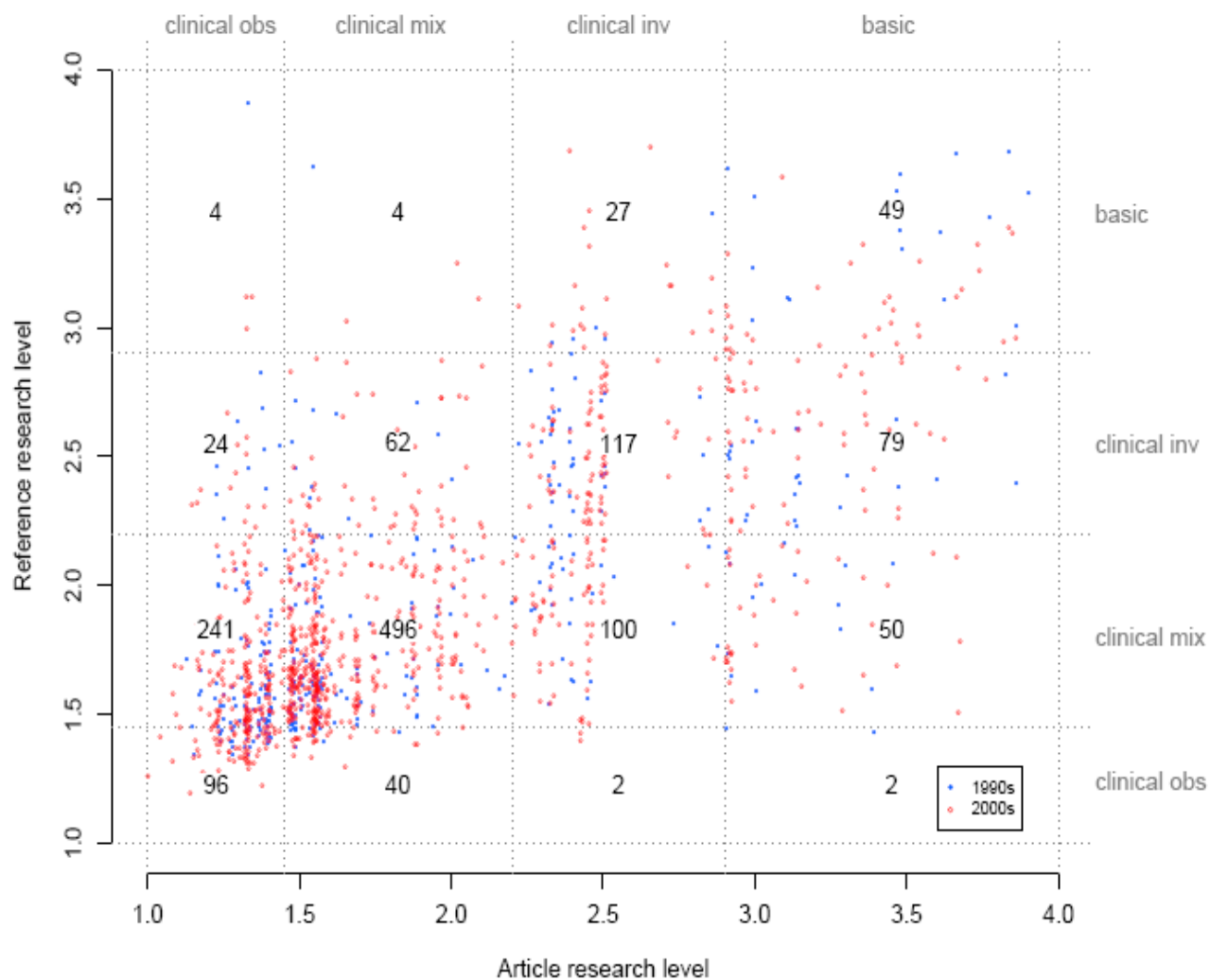


Figure 6: Mean research levels of references in SGDP articles by research level of article. The number in each cell is the number of articles in that cell. There are, for example, 496 SGDP articles classified as clinical mix with references to articles classified as clinical mix, and 62 with references to articles with a clinical investigation classification.

This analysis shows that, at the clinical end of the spectrum, there is a broad correspondence between the level of the referencing article and the level of the cited article – that is to say that publications in the clinical research area tend to cite more references from papers published in journals specialising in clinical research. However, as one moves towards the basic end of the spectrum, the research levels of referenced articles becomes more dispersed. Of SGDP articles within the clinical mix category, about 80 percent (496) cite articles in the same category, while for articles published in journals specialising in basic research, the proportion is around 27 percent; in fact, the greatest number of articles cited by SGDP publications in this area are from the clinical investigation category (78). In terms of translation undertaken in the research publications of the SGDP authors, the main direction of movement is not so much ‘from bench to bedside’ as ‘from bedside to bench’: the publications reporting basic research are drawing upon a relatively greater proportion of more clinical material than in the other direction, where there is relatively little use of basic research papers in those published in journals classified as clinical observation and clinical mix.

Impacts of SGDP research – citation analysis

The results from the analysis of references from SGDP articles shows where SGDP research *comes from* – that is to say, the field of findings that it draws upon and addresses in its research. An analysis of where SGDP articles are cited shows where research results *go* – that is to say, the fields where it has an impact.

For this part of the analysis, because of the practical constraints of searching and checking search results, it was necessary to sample from the set of SGDP records: 100 records were chosen at random from records having citations per year figures of greater than or equal to the mean of 2.7 citations per year. Citation searches were run on the SCI and SSCI databases for each of these, resulting in a set of 8731 records of citations to articles published by researchers at the SGDP.

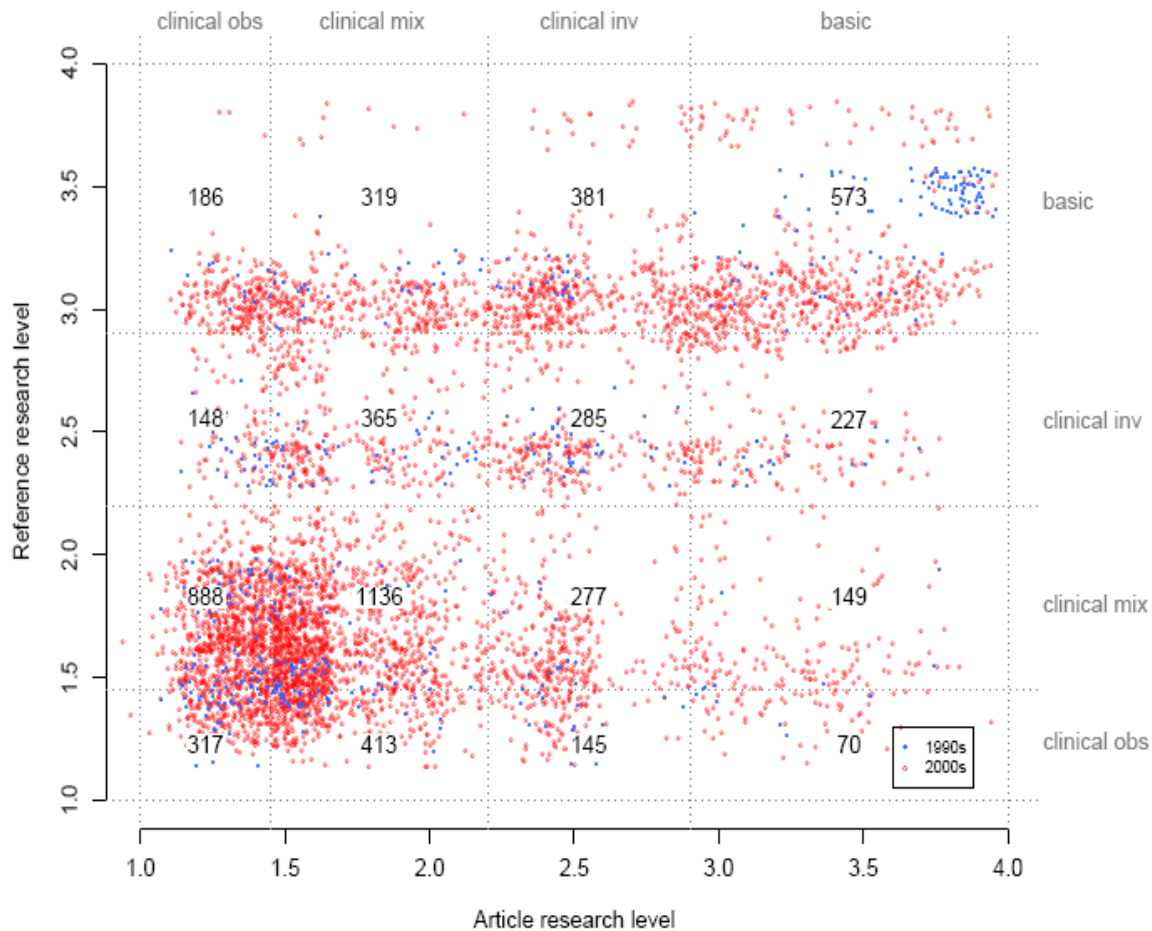


Figure 7: Mean research levels of articles citing SGDP articles (Article research level) by research level of SGDP article. Derived from cited reference searches for a random sample of 100 SGDP records cited more than 2.5 times per year.

The results are shown in Figure 7. What is striking in this plot is that it is dominated by the same clustering around the 1.5 level – that is to say that SGDP research is largely taken up by those working towards the clinical end of the spectrum. However, there are clear patterns of citations to SGDP articles across the whole research level range. This is most particularly evident for citations to SGDP articles of a research level of around 3.0, suggesting that basic findings from the SGDP are being taken up by others conducting ‘clinical investigation’ forms of research. The lowest frequencies are to be

found in the bottom right of the plot: fewer articles in the basic areas are citing clinical articles from the SGDP – so that form of reverse translation, from clinical findings at the SGDP to basic research undertaken by others is relatively less frequent. However there is some evidence that this has changed over time. If one looks at the difference between the 1990s (in blue in the plot) and the 2000s (in red) one finds that there has been a change in the distribution over time. In the earlier period, basic research articles, and especially those close to a research level of 4.0, tended to cite basic research articles from the SGDP.

Overall, however, in terms of volumes of articles citing SGDP articles the most dramatic change has been the growth of citations in the clinical mix zone of the spectrum. This can be seen in Figure 8, which shows changes in frequencies for each CHI research level, and Figure 9, which shows changes in proportion over time.

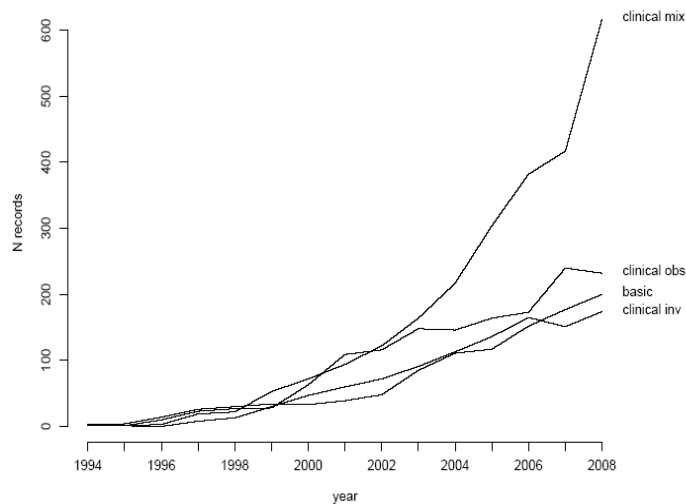


Figure 8: CHI research level counts of citations to SGDP articles by year.

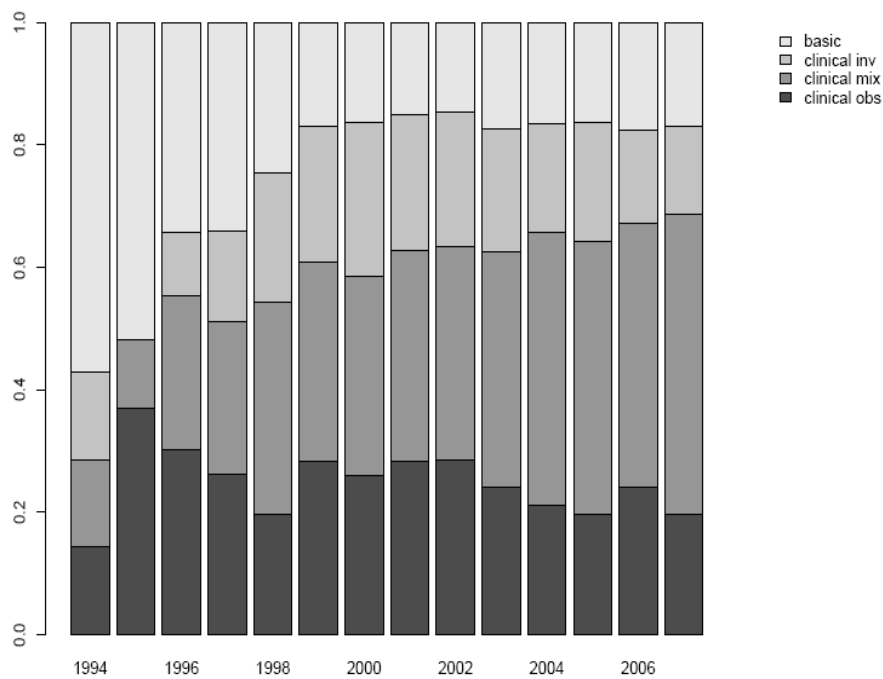


Figure 9: CHI research levels of articles citing SGDP articles by year (proportions)

External collaboration from researchers at the SGDP

Another way in which we can explore translation is by investigation patterns of collaboration in research, and in particular by examining the extent to which researchers at the SGDP collaborate with those positioned at different points on the spectrum from clinical to basic research.

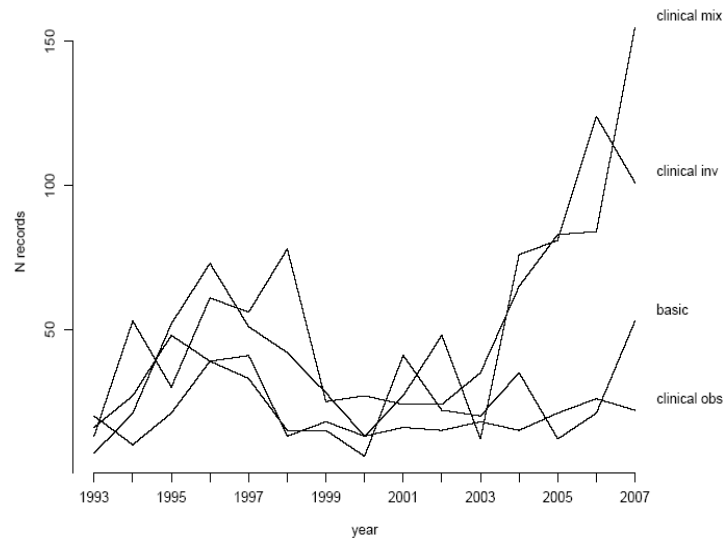


Figure 10: CHI research levels of collaborators with SGDP authors by year.
Based on a random sample of 100 SGDP records.

In order to explore this, we selected a random sample of 100 records and retrieved two further sets of bibliographic records: records with collaborators named in the SGDP records, and records to establish the research levels of journals in which these collaborators published, where the research level of that journal had not been previously calculated. Figure 10 shows an increase in the clinical mix category among articles published by collaborators with researchers at the SGDP authors similar in relative magnitude to that for citations to SGDP articles (Figure 8). However there is also a notable increase over time in collaboration with those in the clinical investigation category. On this evidence, in terms of how SGDP researchers collaborate with individuals outside of the SGDP, there has been a movement towards the centre of the research level spectrum.

The balance of basic and clinical publication for individual authors

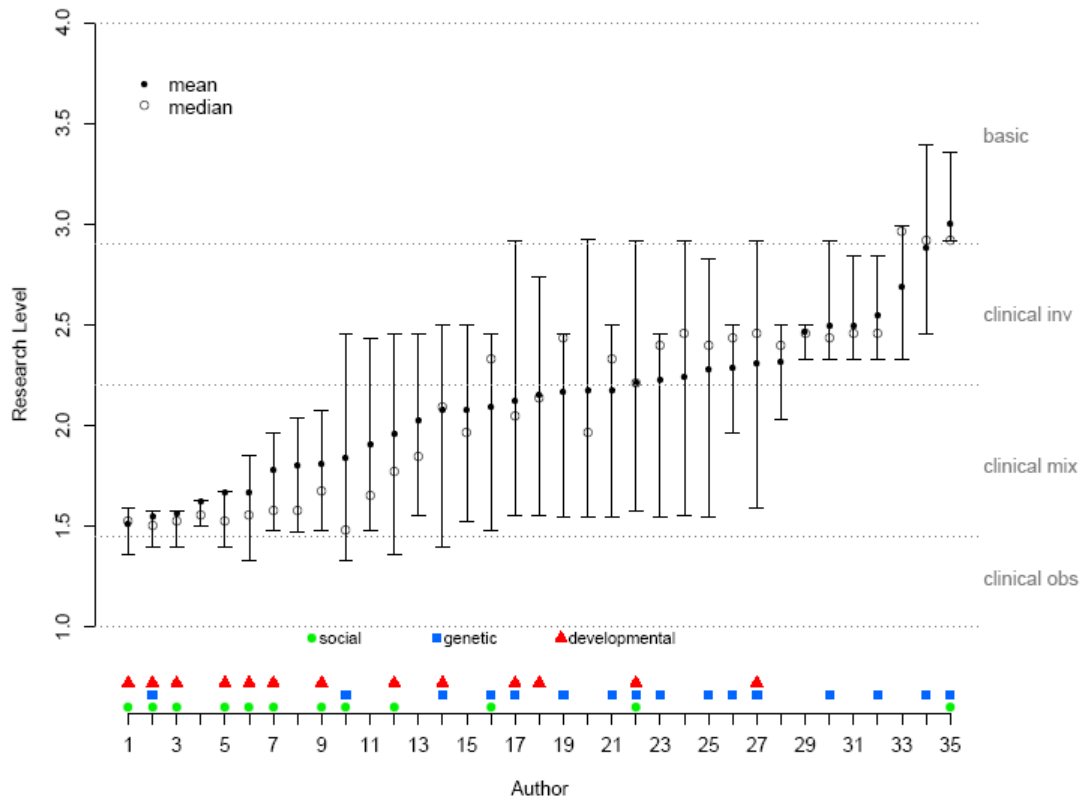


Figure 11: Research level range of SGDP authors, ordered by mean research level.

Another way of analyzing the profile of research conducted by researchers at the SGDP is to examine individual authors and to explore their publication patterns. Are some more varied than others, and is there a relationship between research level and the field within which the author works?

Author research levels were calculated using the research levels of their individual articles. For the analysis, it was necessary to introduce the idea of a research level *range*.

A preliminary inspection of the author research level data showed that many authors spanned a very wide range of research levels: the mean span is 2.3 and many authors have a standard deviation for research level of greater than 0.5. Thus, simple measures such as mean or median are not adequate estimates of an author's average research level.

It would be interesting to undertake a wider analysis of research level ranges of authors, and to undertake some comparative research, to establish what sort of research level distribution is typical for individual authors in particular research fields, and to develop from this a measure of research level range. While it seems that individuals at the SGDP have unusually broad research level ranges, comparative analysis would be necessary to establish the specificity of this finding.

Several methods of calculating the upper and lower limits of the range were explored, including variance and standard deviation. The one that was adopted was to make use of the upper and lower quartiles of the range. This gives, for these data, a conservative measure of the dispersal of an individual's research levels which also retains information about differences in the spans above and below the mean and median research level.

The plot in Figure 11 shows the result of these calculations, ordered by mean research level. The plot also shows at the bottom a classification of some of the authors according to whether their work is in the social, genetic or developmental fields. This classification is derived from a prior piece of bibliometric analysis by an SGDP member (Schalkwyk 2004). This result was shown to some members of the SGDP for their responses, primarily to check that the classification was accurate for each author.²⁴ One individual was reported to occupy a place further to the basic end of the plot than

would have been expected, which led to retrieving the missing records for that individual and re-running all of the research levels analyses.

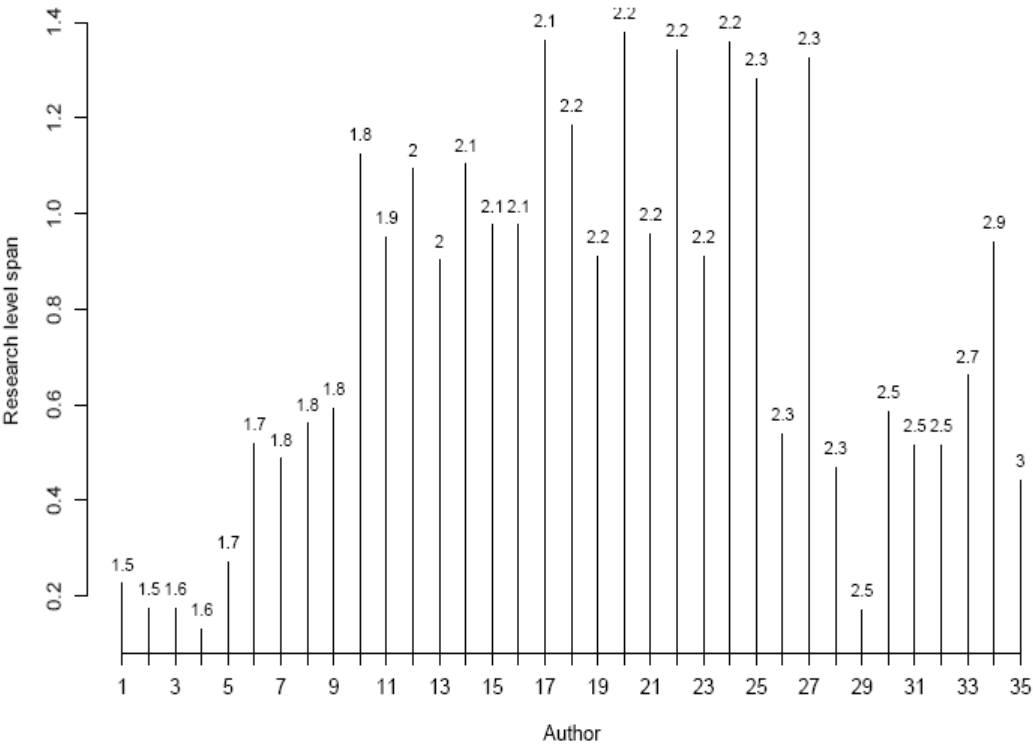


Figure 12: Spans of research level ranges for each author, ordered by mean author research level. The number at the top of each line is the mean research level for that author,

The plot shows that the SGDP has some members with relatively narrow research level ranges at either end of the scale from clinical to basic, with those at the clinical end narrower in range than those at the basic. Figure 12 shows the spans of each author’s range. With two exceptions (individuals 2 and 35 in the plot), there is a pattern of fields that corresponds with these ends of the scale: social and developmental at the clinical end, genetic at the basic. In between, and particularly from author 10 to author 27, one

can see a large number of individuals with mean research levels between 1.48 and 2.46, many of whom also have very wide individual research level ranges: the mean span for this group is 1.1, compared to a mean of 0.35 for authors 1 to 9, and 0.54 for authors 28 to 35. These higher central ranges cover, in some cases, almost two of the CHI research level categories.

There is some evidence, therefore, of translation at the level of individuals – that is to say, of individuals publishing in journals across a wide span of the spectrum from basic to clinical. There are, however, two qualifications to this finding. Those closer to the extremes of the scale are less ‘translational’, and only a very few individuals’ research ranges cross over into the clinical observation level (and even then, only at the extreme ends of their ranges).

Interdisciplinarity and collaboration

An interesting observation came out of discussion with the SGDP about the author research level range plot in Figure 11. It was suggested that it might not be capturing something on the clinical to basic scale, but rather on a scale that had ‘social’ at one end and ‘molecular’ or ‘genetic’ at the other. It might also be that the analysis is also capturing the location of each author on the dimension of inter- and multidisciplinarity: most interdisciplinary individuals also appear to have the broadest research level ranges. Further research would be needed to explore the relationship between these different dimensions, but one can get a preliminary indication of patterns by examining the relationships of collaboration and interdisciplinarity amongst individuals at the SGDP.²⁵

The SGDP is characterized by its interdisciplinary aims: not merely to permute the social, the genetic and the developmental, but to develop an account of gene-

environment interaction that transcends the individual competencies of each individual SGDP researcher:

[interviewer] *Previously I'd been thinking about it more like a sort of combinatorics or as a set of permutations of social and genetic and developmental in terms of a dynamic interplay in different ways.*

In the end that's what's going to be underlying the troubles we're trying to investigate.

[interviewer] *So you could have a story to start with genes and goes through the mice and...*

And then goes through the brain and so forth. There are other people here who are doing imaging and trying to see what bit of it is...So that all those biological bits would fit together. And then there are people that are doing proteomics and stuff like that, I don't even really know what the words mean for myself. So there are different stages, and also people like X who is putting imaging and genetics and treatments together, focusing on alcohol and drug problems. The nice thing about that sort of approach is you can know something fairly clear about the environment because the environment is how much alcohol you drink, or how much of the drug you take. That's much easier to quantify than some of the stuff that I do, which is around is your mother nasty to you kind of thing.

There are two aspects to this 'bridge-building': collaboration between researchers and the translation of research across fields and sub-fields within and sometimes outside of the bounds of the social, genetic and developmental.

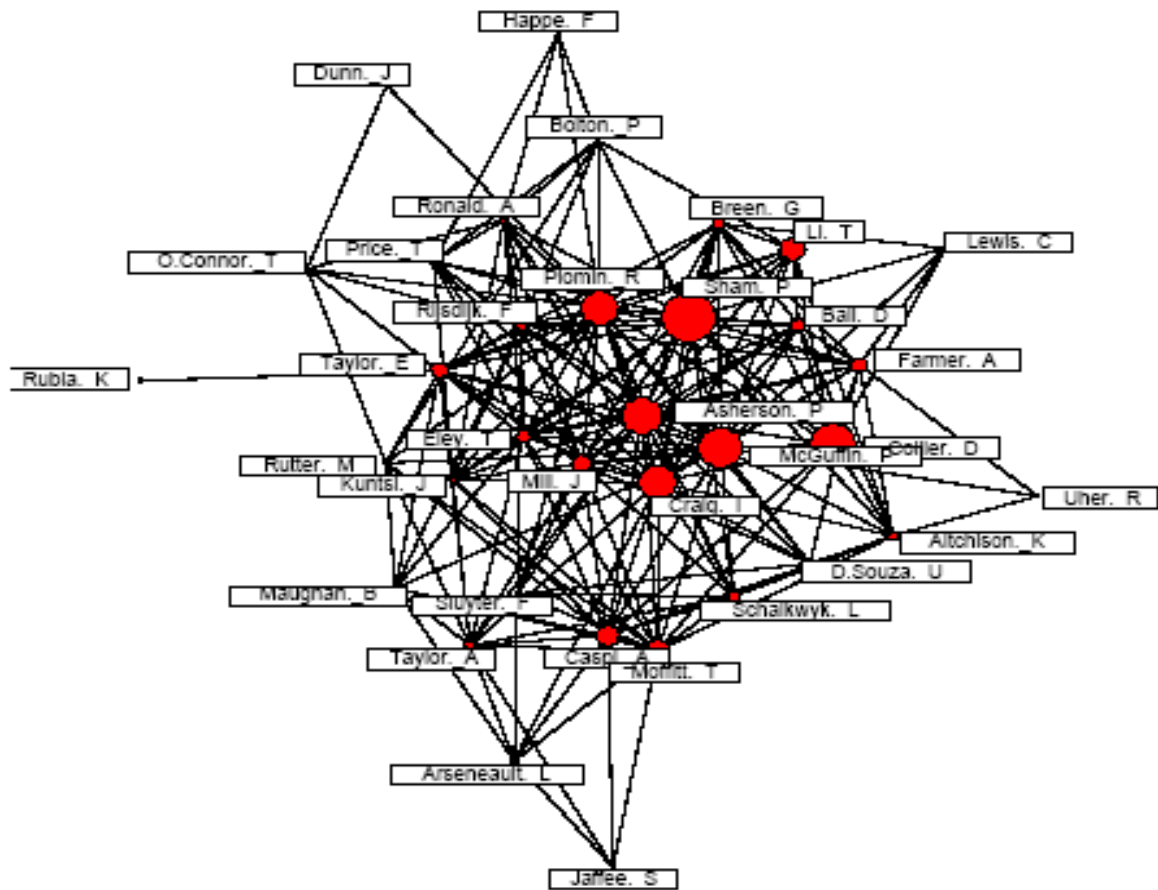


Figure 13: Author collaboration network (all years). The size of the circles at each node is proportional to the network centrality of that individual.

One way, therefore, of finding evidence for this kind of inter- and trans-disciplinary activity is to look at patterns of collaboration between members of the SGDP. Using the bibliographic data, one can derive an author collaboration network such as the one in Figure 13. In this diagram, the size of each vertex represents the network centrality of the author according to the number of collaborations they have with other authors. Figure 14 shows how this network has developed across time, showing an increase in

the number of vertices and a pattern of increasing collaboration amongst members of the Centre.

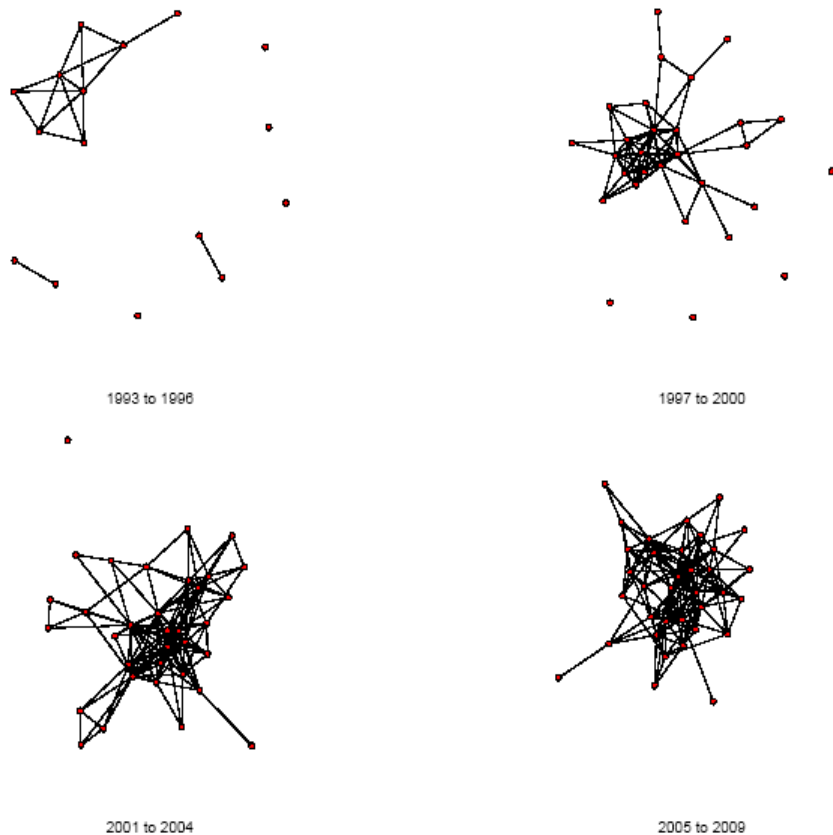


Figure 14: Author collaboration network by years

A similar analysis was done using the subject categories applied by the SCI to journals. These were chosen rather than keywords in order to establish a map of publications in different journal types. The network diagram in Figure 15 shows a subject category network over all records in the database (excluding the very general category of

‘psychiatry’, which appears in every record. It shows the interrelationships between different categories. There is a strong core of ‘neuroscience’, ‘behavioral sciences’, ‘genetics and heredity’ and ‘psychology, multidisciplinary’, which is unsurprising given the purpose of the centre and its multidisciplinary aims.

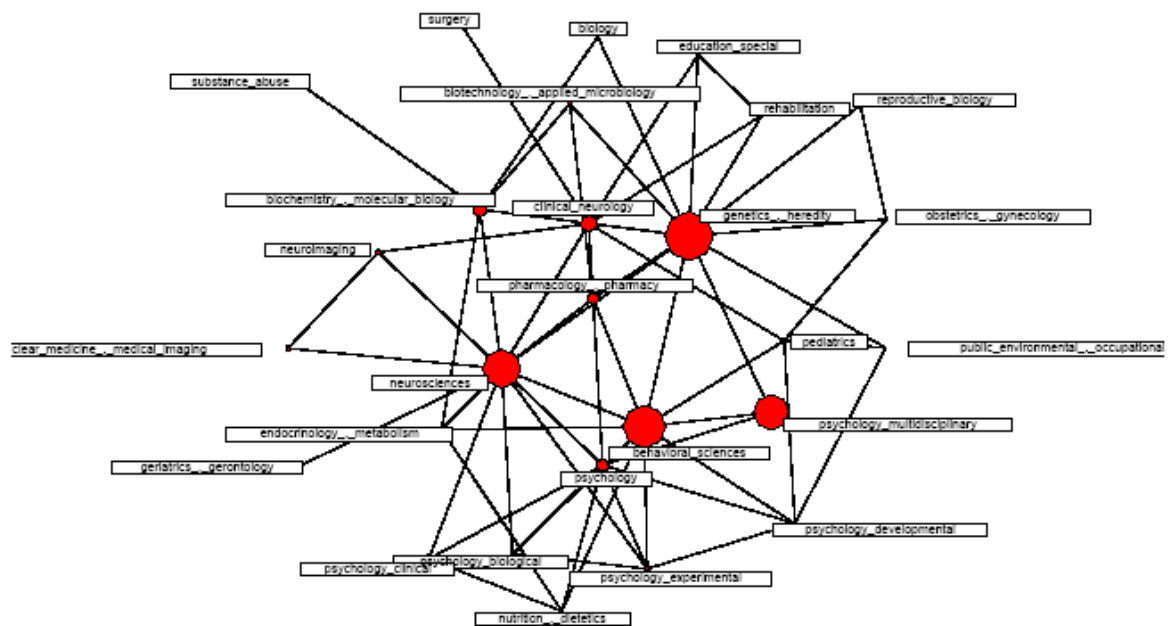


Figure 15: Subject category network (all years)

A breakdown of the network by three-year intervals shows a pattern of growth across time from a few subject category linkages in the 1990s to a tightly interwoven network in the late 2000s.

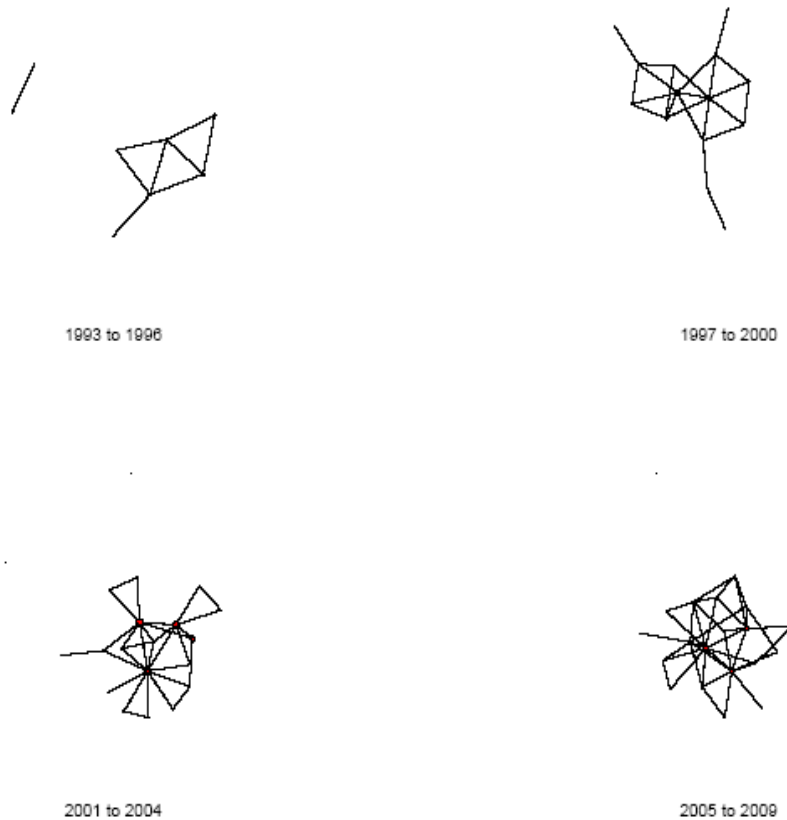


Figure 16: Subject category network by years.

Changes in both the collaboration network and the subject category network suggest an increasing interrelationship between individuals at the SGDP in terms of who they

work with within the centre, and of what they work on. One could interpret this as a positive outcome of the co-location of the researchers within a single purpose built building created for the SGDP. These results must, however, be interpreted with some caution. Such patterns of change over time may be quite typical of how collaboration especially, but interdisciplinarity too, develops in a research centre: since people form research centres and join ones already existing in order to work with others, it is, perhaps, inevitable, that such patterns of development occur. This is another area in which further bibliometric research is required, to establish a model of normal collaborative and interdisciplinary network development.

Nonetheless, it is reasonable to point out that these networks could have developed differently: one could plausibly imagine that, in the absence of a high degree of collaboration and interdisciplinarity, three distinct networks might have emerged: a social one, a developmental one and a genetic one.

Discussion

The analysis presented in this chapter has concentrated on addressing the Cooksey 'gap' in translation, using the concept of research level as its main tool. The data for the analysis and the results from their analysis have involved peer-reviewed articles represented in the SCI and SSCI. Initially, it was intended to broaden this analysis out from peer-reviewed journals, following Lewison's (2005) article *Beyond SCI citations: New Ways To Evaluate Research*, in order to explore the 'pathways' of research out into national and international standards, government policy documents, clinical guidelines, textbooks, and newspapers. However, this proved to be impossible within the constraints of the project: gathering good data in these areas and solving some difficult problems of record-linkage (connecting bibliographic data with data from each of these data-sets) is extremely labour-intensive and time-consuming.

Nonetheless, the analysis presented here provides some indication of the extent to which the SGDP, as a research centre does, or does not, overcome the translational gaps that were identified in Cooksey.

The pattern of SGDP publications shows a strong emphasis in three areas that may broadly be defined as 'clinical', 'mixed' and 'basic'. The basic end tends not toward the most basic research in neuroscience, but toward the clinical investigation level. The most clinical of the publication output of the SGDP, which dominates the overall profile, is also not at the extreme end of the spectrum. There is a noticeable absence of publications in journals located at the very clinical end, and this is also represented in references from and citations to SGDP publications – the focus is located somewhere between clinical observation and clinical mix. This is not surprising: it is consistent with the SGDP's espousal of 'experimental medicine' as its brand of translation (Rutter and Plomin 2009).

In terms of the research drawn upon in SGDP publications, the most salient feature, which has developed over time, is evidence of 'bedside to bench' translation: basic papers drawing on more clinical ones.

In terms of where SGDP articles have their impact - where research goes next - there is a broad range of destinations. Much research stays in the same region, particularly in the research level 'heartland' at around 1.5, with basic findings appearing to be the most 'translated', since these are taken up evenly over the whole range of research levels. Comparing the 1990s with the 2000s shows that much of this propagation of basic research findings has happened in the latter decade: in the 1990s, there is a tight clustering of citer research levels around the research levels of SGDP articles that they cite. The overall picture, however, is of an increase in the clinical mix level of citations to SGDP articles.

Individual authors at the SGDP show wide research level ranges, particularly spanning the clinical investigation/clinical mix levels. These broad spans may be interpreted as high degrees of translational activity, and are associated with the most interdisciplinary individuals, which suggests that to some extent translation is associated with interdisciplinarity and collaboration. Notwithstanding the absence of an underlying model of research centre collaboration, the analysis of collaboration and interdisciplinarity amongst SGDP members corroborates this association.

More general bibliometric work is needed to establish models and distributions. What, for example, is the long-term research level trend in the biomedical literature? What citation trends exist? Can these different elements be put together into a bibliometric translational model, preferably with a time dimension? Research level classification using Lewison and Paraje's (2004) method provides a useful tool for analyzing translation since it allows one to examine movement across the 'bench to bedside' spectrum. Establishing these models would allow the development of an evaluative bibliometrics of translation based upon research levels.

6. CONCLUSIONS

Our overall conclusion, arising from this research, is that Cooksey was right in arguing that more basic research on the process of translation needs to be done. Such research needs to explore, describe and analyse the diverse and often conflicting views of the nature and value of the translational imperative. Merely to invest in translation, or to re-badge funding as 'translational' is likely to be counterproductive: merely emphasising the importance of something no one can define properly is unlikely to get results. Until quite recently, management consultants in this area, such as Ernst and Young, tended to view the problem in very conventional managerial terms, arguing the goals need to be set, managed, achieved and monitored. But in our view, this approach is unlikely to succeed until we have a better understanding of the basic problem. Recent developments at the MRC, and in the National Institute of Health Research, indicate that a more complex and nuanced understanding of the process of translation is taking shape, more aware of the institutional forces that need to be mustered and shaped in order to nudge basic researchers, research funders and clinical practitioners into closer and more productive relations.

Our bibliometric analyses show that the publications of SGDP researchers do indicate a significant interest in translational potential, the majority being directed to the borders between the clinical and clinical mix categories, indicating a concern with the potential applicability of the findings and to communicating research results into the clinical domain. This is consistent with the espousal of many researchers at the SGDP with a particular version of translation, that is to say, the model of 'experimental medicine' set out by Michael Rutter and Robert Plomin (Rutter and Plomin 2008). While there is considerable individual variability among researchers, as one would expect from our qualitative research, there is an increase in such publications across the period from 1990 to the present, it is also clear that the collaborative emphasis of the SGDP, embodied in the very design of the institution and its physical form, has facilitated an

increasing level of interdisciplinary collaboration between research on the social, developmental and genetic aspects of behaviour among researchers based at the SGDP, and this in itself embodies on key dimension of translation. However it also suggests that, in developing robust indicators of potential translational value in work supported by the MRC, it would be insufficient to focus solely on publication outputs over the short or even medium term. It is clear from our work in this area that there is a need to develop more sophisticated and sensitive methods for capturing the impacts of research funding in relation to the generation of economic and health benefits, and the multiple forms that such impacts can take. The pathways from research outputs to policy are notably difficult to capture, given the different timescales on which they operate, the heterogeneous and often non-rational factors that affect the take-up of research findings in debates over policy, and the socio-political and economic vicissitudes that shape the process of policy formation and change.

In this context, we argue that one central way in which we can understand the success of models of translation as they affect, or capture, the conduct of research itself, is to undertake a deeper exploration of the cultures, beliefs and expectations of the actors involved in 'making translation happen'. Our qualitative research confirms the value of going to the situated users, that is to say, the researchers themselves, and asking for their 'embedded', first-hand, or 'coal face' models of translation. The 'embedded' translators are in a very good position to offer quite nuanced and sophisticated models of translation that differ considerably from the mainstream varieties, which are largely fictive (and which they rightly reject). While our own project here is preliminary, we believe it demonstrates that these insights need to be systematically collected and compared, and then used as the basis for a discussion of translation that is empirically-informed and data-led, rather than being led by wishful thinking.

The situated informants (interviewees) show us that much of the official language of translation, and the associated models of the process, is quite a different thing from its

‘actual’ workings in the lives and decisions of researchers. As Power’s research on audit confirmed with respect to earlier attempts to use measures of accountability and techniques of audit to influence organisational change, translational thinking does not exist in a unified form, or as a single rationality, within organisational cultures, such as that of the Institute of Psychiatry. As far as practicing researchers and research is concerned, there are, in effect, two translations in process: first, translation as a managerial discourse and government strategic objective; second, translation as an actual set of processes and outcomes. The former is aspirational and ‘strategic’, whereas the latter is often a retrospective re-description of specific processes and research pathways. Our interviewees describe, often in nuanced and sophisticated terms, the ways in which these, and other features of the two translations, in fact rarely converge.

It is clear from our research that there are multiple models of translation at work among researchers, and multiple overlaps and divergences between researchers and those in managerial and policy roles. This plurality arises from the research and institutional context itself, and the variety of values, roles, orientations and objectives of the different participants. In our view such plurality is inescapable. Hence we would argue that the aim of government and research funders should not be to seek to reconcile all of these diverse translational rationales, but to ‘adjust’ them to the different contexts for which they are relevant. Government does not need to utilise the same definition of ‘successful translation’ as those adopted by the researchers in any area, but they do need something to enable them to intervene in these situations and shape them in particular directions, while recognising their specificity. In this sense ‘translation’ comes to resemble ‘transparency’ – framed in a very wide and inclusive sense it can become a language to which all can subscribe, and within which all can adjust their ways of working so that they are loosely coupled together towards the same overall ends.

A second conclusion we would draw is that there are significant dangers for organisations such as the Institute of Psychiatry, both in complying too closely with the translational imperative, and in neglecting it. Under the current frameworks for governing organisational life and professional activity, within which the audit ethos has become a core element within public discourse and a key means of judging moral value, the need to respond to auditing measures of translational impacts is vital if an organisation is to win resources, maintain its legitimacy, and increase its influence in the fields to which its work is directed. Paradoxically, however, these responses run a risk of becoming over-responsive, to the extent that, if applied mechanically or ritualistically, they run the risk of damaging the very diversity of research cultures that makes them functional and valuable – based, as these are, in the real lives of researchers such as those we have interviewed, on more serendipitous and inchoate forms of connection, influence and association.

As a result, ‘making translation happen’ is in part a matter of trying to achieve a fit between a version of what scientific research does, and different ‘contexts of expectation’. In part, this confirms a view argued by those who work in ‘the sociology of expectations’ – that part of the role of both scientists and governments is to ‘manage expectations’ as much as ‘delivering outputs’. From this perspective, one can argue that by placing so much emphasis on the imperative of translation, the government and funding bodies may be stoking expectations, increasing pressures to exaggerate or oversimplify the pathway from basic research to clinical application, and in doing so, ultimately leading to disillusionment among those whose trust in the power of science to improve human affairs may already be somewhat fragile.

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APPENDIX ONE: INTERVIEW TOPIC GUIDE

We are conducting research funded by Medical Research Council on translational research. The research involves a case study of the Social, Genetic and Developmental Psychiatry centre to identify processes of the translation of basic research findings and also to identify barriers to such translation.

Confidentiality

My background

Topics:

- Brief description of current research activities. Funding.
- Values, motivations: why do you do the kinds of research that you do?
- How did you come to do it?
- Interactions between the laboratory and the clinic?
- Interdisciplinarity: how important is the interdisciplinarity of the centre to you?
Examples?
- What do you understand by the term translational research?

Understanding of the concept of translational research;

[stimulus]The process of the bidirectional transfer of knowledge between basic work (in the laboratory and elsewhere) with that of the person, in health or disease.

- How much does translation figure in how you do research? [shaping research problems, finding funding]

Perceptions of the process leading from identification of research problems, through funding, to translation;

- Do you have to justify your research in terms of translation?
- What is translatable in your current research?
- Impact of work at SGDP: yours and others

Perceptions of key research papers and findings from the SGDP that have had impacts in terms of human health and economic competitiveness;

Perceptions of research pathways whose initial promise was not fulfilled, and of the problems of identifying more or less productive research pathways in advance or at different stages in the research process.

ENDNOTES

- ¹ From the perspective of this present research it is relevant to note that Sir Michael Rutter, a senior member of the SGDP and a former Director (until 1998), was later to be the author of a paper evaluating the relevance of the idea of translational research for neuroscience, which we discuss later in this report.
- ² Some further details of SGDP, size, staffing, research grants awarded etc to be inserted here
- ³ An indicator of its growing salience is the number of results per year found by a search for 'translational research' 2 in the Social Sciences Citation Index. It is only in the 1990s that the term appears there at all, and of the total number of results (2223), ten percent (217) are in the 1990s, and there are 472 results for 2007 (roughly twenty percent). A similar trajectory can be found searching the Nexis News database, which covers newspaper reports.
- ⁴ There are translational research centres and institutes in many cities in China, India, Singapore and elsewhere. Indeed many Asian countries believe that they can become the international leaders in translational research in biomedicine.
- ⁵ We have drawn on various reviews of this history, notably Malenschein et al. (2008) who provide a very useful overview and critique of the current emphasis on translational research.
- ⁶ See for example the Wellcome Trust press release announcing the publication of their "largest ever study of the genetics of common diseases" in June 2007 - <http://www.wtccc.org.uk/info/070606.shtml> - consulted 23 November 2009.
- ⁷ <http://www.loc.gov/loc/brain/proclaim.html>
- ⁸ This, of course, has been the hope ever since the term 'biomedicine' was coined to indicate this novel alliance between practices for the treatment of pathology and basic knowledge of biological processes (see Keating and Cambrosio 2003).
- ⁹ www.nihroadmap.nih.gov/overview.asp
- ¹⁰ Thanks to Grant Lewison for this point.
- ¹¹ http://www.nihr.ac.uk/about/Pages/about_information.aspx
- ¹² We also draw in general terms upon the work of the IoP itself in its workshop on translation.
- ¹³ One should, of course, point out that some action was taken at different points along this timeline, for instance restrictions of advertising, health warnings and price adjustments.
- ¹⁴ Note that the Royal Institution has a press bureau, but it is not an agency of universities.
- ¹⁵ Records were parsed, cleaned and analyzed using software developed by the author in Common Lisp and in the R system for statistical computation and graphics (R Development Core Team 2008).
- ¹⁶ There is, of course, a third limitation of this method – that is to say that it applies not to individual papers but to journals. It is possible to classify papers individually, but the advantage of classifying them in terms of the journals in which they are published is that it can serve as a proxy for the audience to which the paper is considered relevant. Of course, this journal based form of analysis is becoming less relevant at a time when internet availability of full text articles coupled with search engine capacities means that one can read papers with little idea of the journal in which they are published.
- ¹⁷ Of course, to some extent the publication profile from any research centre may be influenced by the popularity of particular journals as potential publication outlets for members of that

Centre, but it is unlikely that this will shape the distribution as a whole. A further factor affecting the distribution over time is that fact that new, and sometimes popular, journals have come on stream during the period of analysis. However we do not believe that this affects the basic rationale for analyses using this method.

18 <http://www.wiley.com/bw/journal.asp?ref=0021-963077>

19

http://www.elsevier.com/wps/find/journaldescription.cws_home/506091/description#description

20 <http://www.ovid.com/site/catalog/Journal/268.jsp>)

21 <http://www3.interscience.wiley.com/journal/117928900/grouphome/ProductInformation.html>

22 <http://www.nature.com/mp/index.html>)

23 <http://www.springer.com/public+health/journal/10519>

24 The plot shown to the SGDP included the names of the individuals; in this report these have been replaced with numbers to preserve anonymity.

25 This analysis replicates and extends to 2009 some of Schalkwyk's (2004) work.